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VOLUME XXIII NUMBER 3

DISEASES

of the

CHEST

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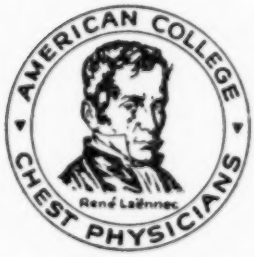

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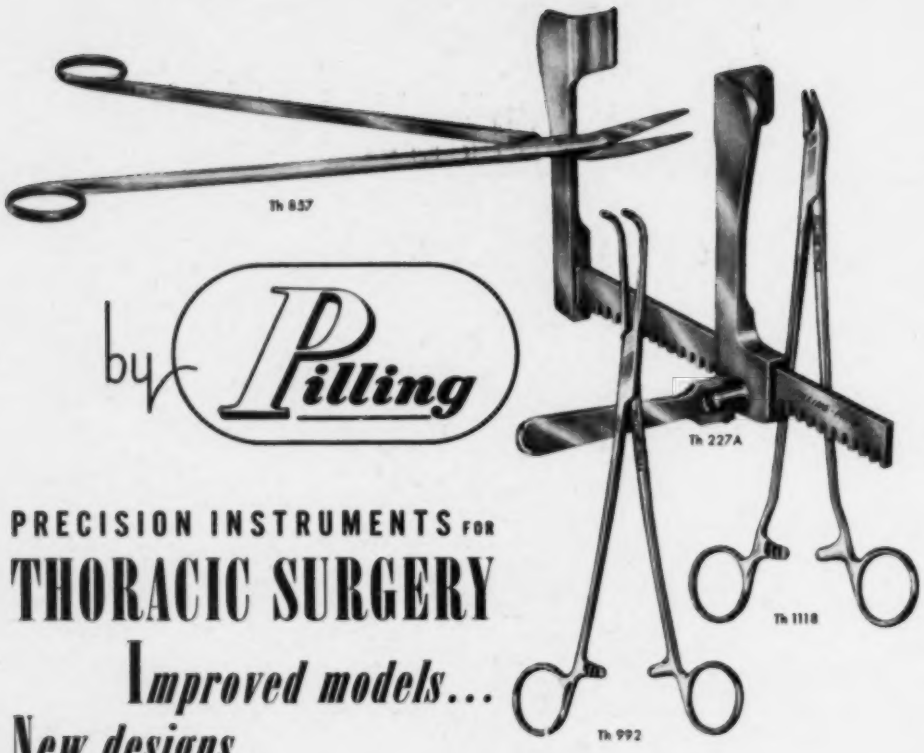

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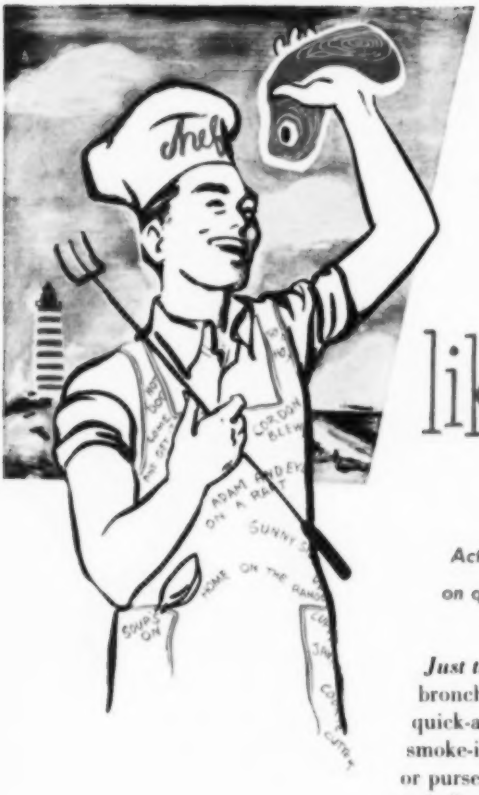

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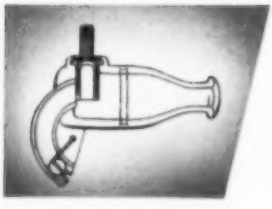

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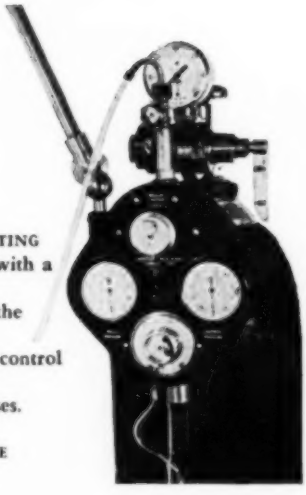

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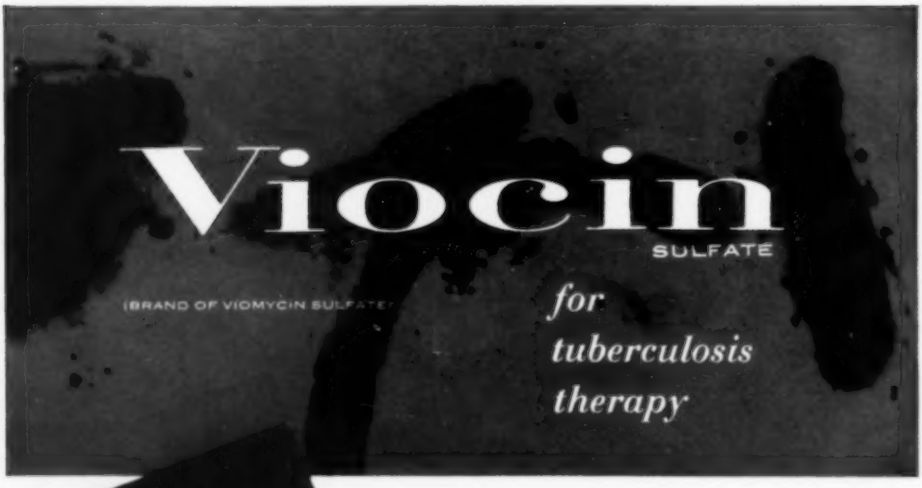

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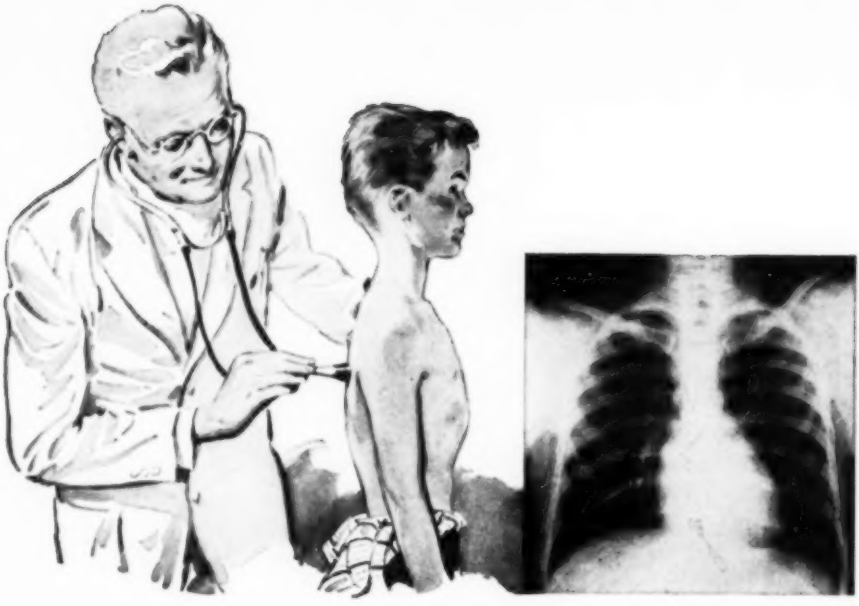

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DISEASES *of the* CHEST

VOLUME XXIII MARCH 1953 NUMBER 3

Intermittent Viomycin Therapy in Pulmonary Tuberculosis*

Employed Singly and in Combination with Intermittent Streptomycin or Daily Para-aminosalicylic Acid

FORREST W. PITTS, Capt., MC, USA, EDWARD T. O'DELL, Capt., MC, USA, MARTIN J. FITZPATRICK, Capt., MC, AUS, WILLIAM E. DYE, Capt., USAF (MSC), FREDERIC J. HUGHES, JR., Lt. Col., MC, USA, and CARL W. TEMPEL, Col., MC, USA, F.C.C.P.

Denver, Colorado

Clinical and laboratory studies have shown that viomycin possesses antituberculous activity and appears worthy of further clinical trial.[1-6] Daily intramuscular administration of 30 to 75 milligrams of viomycin per kilogram of body weight has resulted in significant drug toxicity[7,8] and bacterial resistance. Previous experience with streptomycin has revealed that the problems of drug toxicity and bacterial resistance may be materially reduced when the principle of intermittent therapy is employed.[9] This, and the known similarity of many biologic properties of viomycin and streptomycin have provided the rationale for the regimens used for the treatment of 80 patients with pulmonary tuberculosis reported in this paper.

Material and Methods

Thirty-six patients received one gram of Viomycin (VM)** at 8 A.M. and 12 noon and one gram of streptomycin (SM) at 8 P.M. every third day. A second group of 22 patients received two grams of viomycin every third day (8 A.M., 12 noon) and 12 grams of para-aminosalicylic acid (PAS) daily. The third group consisted of 22 patients who received two grams of viomycin every third day administered at 8 A.M. and 12 noon. Viomycin and streptomycin were administered intramuscularly and para-aminosalicylic acid orally. Duration of therapy in all cases was 120 days except in one patient in whom drugs were discontinued because of toxicity.

All patients had moderately or far advanced disease with sputum positive by culture for tubercle bacilli prior to treatment. No previous chemotherapy for tuberculosis had been administered. All were male and 87 per cent were

*From the Chest Disease Section of the Medical Service and the Research and Development Branch of Fitzsimons Army Hospital, Denver 8, Colorado.

**Viomycin was supplied through the courtesy of Charles Pfizer and Company, Inc., Brooklyn, New York.

white. Ages ranged from 19 to 58 years with an average of 31. Table I summarizes the background factors.

In general, the disease was severe as illustrated by the high proportion of cases that were far advanced, bilateral, and cavitary. The distribution of the clinical pathologic type of disease, determined largely by serial roentgenograms, is shown in Table I. The groups were similar, except for a higher proportion of mixed new and old disease (Type V) in the 22 patients who received viomycin alone.

Patients were evaluated for clinical, roentgenographic, bacteriologic responses, and drug toxicity. Clinical criteria were: alterations of temperature, change in sputum volume in excess of 30 cubic centimeters, and variations of weight in excess of five pounds. Patients were considered improved if there was a favorable change in any one of these factors without worsening in the remainder. Chest roentgenograms were evaluated by at least three physicians in terms of trend of pulmonary lesions and

TABLE I

BACKGROUND FACTORS ON 80 PATIENTS TREATED WITH INTERMITTENT VIOMYCIN THERAPY

REGIMENS		VM 2 GM Q3	VM 2 GM Q3 SM 1 GM Q3	VM 2 GM Q3 PAS 12 GM QD
NUMBER OF PATIENTS		22	36	22
AGE:	Range	19-58	19-56	19-56
	Average	33	29	32
RACE:	White	9	32	18
	Non-white	13	4	4
SEX:	Male	22	36	22
	Female	0	0	0
EXTENT OF TUBERCULOSIS:				
Moderately advanced		9	24	11
Far advanced		13	12	11
Unilateral		11	18	5
Bilateral		11	18	17
Cavitary		18	28	14
Non-cavitary		4	8	8
CLINICAL PATHOLOGICAL TYPE DISEASE:				
I New Resolving (exudative)		0	4	2
II New Poorly Resolving (caseous pneumonic)		1	0	0
III New Resolving and Poorly Resolving		11	18	15
IV Old Non-Resolving (fibrocaseous)		0	2	0
V Mixed New and Old		10	12	5
ROENTGENOGRAPHIC TREND PRIOR TO THERAPY:				
Regressive		8	6	3
Stationary		12	25	15
Progressive		2	5	4

persistence of cavity. Trend was defined as marked, moderate or slight improvement, no change, or worsening. Marked improvement referred to complete or almost complete resolution. Minimal but unequivocal degrees of resolution were recorded as slight improvement. Worsening was defined as any degree of extension of the disease in any part of the roentgenogram even if other areas were improved. Presence of cavity was recorded if the outlines could be clearly seen.

Bacteriologic studies consisted of sputum and gastric cultures taken at two-week intervals. All positive cultures were tested for sensitivity to 0, 10, 25, 50, 100 and 200 micrograms of viomycin per milliliter of Herrold's egg yolk agar medium. Of the group that received streptomycin or PAS, sensitivity studies to the respective drugs were carried out to 0, 1, 10 and 100 micrograms per milliliter.

All patients were observed for evidence of clinical toxicity. At intervals of 14 days the following laboratory procedures were performed: complete blood count, urinalysis, serum potassium, serum calcium, and urine calcium (Sulkowitch). Monthly serum chloride, serum phosphate, carbon dioxide combining power, bloor urea nitrogen, electrocardiogram, cephalin flocculation, and sedimentation rate were determined. At intervals of every two months a total protein, albumin and globulin determination, and bromsulfalein test were performed. Prior to the institution of drug therapy, at completion thereof (120 days), and two months post-therapy the following were performed: urine concentration test (Fishberg), 15 minute PSP excretion, urea clearance, audiogram, and caloric vestibular test.

All patients were on uniform bed rest during the period of evaluation, but no other form of therapy was employed.

Observation and Results

Clinical evaluation: A satisfactory clinical response was noted in almost all patients on the three regimens (Figure 1). The small percentage of patients who showed worsening is noteworthy. The response to viomycin alone of a patient with moderately severe laryngeal tuberculosis was favorable within a period of six to eight weeks.

Roentgenographic evaluation: Serial x-ray films for one to three months prior to chemotherapy were available in all cases. Pre-treatment x-ray trend was similar in all three groups (Table I).

Roentgenographic response is shown in Figure 2. From 77 to 95 per cent of the patients in all groups manifested improvement, and from 0 to 9 per cent showed worsening. The proportion of patients showing marked or moderately favorable trend following treatment with viomycin alone (9 per cent) was noticeably smaller than in the corresponding groups treated with viomycin and streptomycin (39 per cent) or viomycin and PAS (19 per cent). Apparent cavity closure occurred in only one of 18 patients treated with viomycin alone, in six of the 28 patients treated with viomycin and streptomycin, and in one of 14 patients treated with viomycin and PAS.

Clinical toxicity: The time and route of administration of the three drugs has provided a reasonably accurate means of delineating untoward drug

reactions specifically caused by viomycin. Two patients experienced nausea and vomiting which was distinctly related to the daily oral administration of PAS; all other manifestations of toxicity have been attributed in whole or in part to viomycin. Although streptomycin or PAS may have been responsible for some of the clinical and laboratory toxicity that has been arbitrarily attributed to viomycin, it is noteworthy that the incidence and severity of toxicity did not vary among the three regimens.

Toxicity was notably related to one of the two lots of drug* employed in this study. The disproportionate incidence and severity of toxicity encountered with different lots of viomycin as well as the high incidence of pain, fever, and allergic phenomena suggest that a considerable portion of the clinical toxicity was not inherent to viomycin proper. Thus, in many respects, current experience with viomycin has paralleled clinical problems

*Designated as Lot A and Lot B in this report.

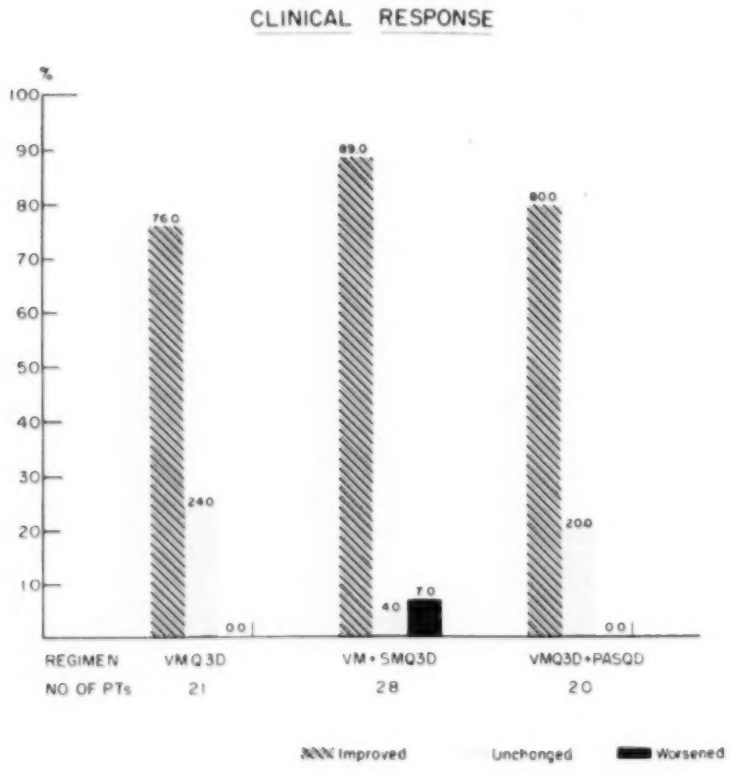

Figure 1 Evaluation After 120 Days Of Drug Therapy, Of All Patients Symptomatic At Start Of Therapy.

FIGURE 1

which were encountered when streptomycin initially became available. However, it is unlikely that all viomycin toxicity was due to impurities.

Clinical toxicity was common and appeared in slightly over one-half of the patients treated (Table II). In most instances it was transient, of minor nature, and required only symptomatic measures for control. Fourteen patients (18 per cent) had reduction in dosage or brief interruption of drug therapy to alleviate side reactions, but treatment was then continued without incident in every case. Severe toxicity which necessitated discontinuing viomycin was encountered in only one patient.

Pain: All patients complained of irritation at the site of intramuscular injection of viomycin, but pain was not recorded in this evaluation unless

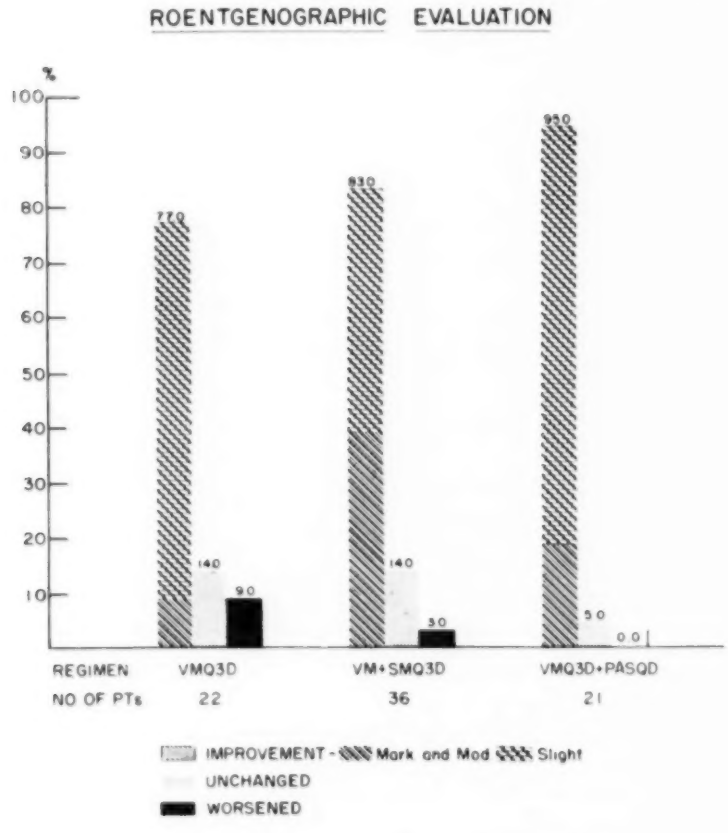

Figure 2. X-Ray Response After 120 Days Of Intermittent Viomycin Therapy, Employed Singly Or Combined With Intermittent Streptomycin Or Daily PAS.

FIGURE 2

accompanied by objective findings such as local tenderness or induration. Interruption of drug therapy for seven to 10 days was required for seven patients because of local pain. Early experience showed that viomycin was more irritating if inadvertently injected subcutaneously as illustrated by one patient who developed a sterile abscess in the deltoid area. This latter complication responded to applications of heat, but thereafter the nursing staff adhered to a standard practice of injecting viomycin only into the gluteal muscle area. Pain was twice as common with Lot B which accounted for moderately severe pain in five of seven patients.

TABLE II

CLINICAL TOXICITY DURING INTERMITTENT VIOMYCIN THERAPY

	No.	Pct.
Clinical Toxicity:		
No significant toxicity	34	42
Mild—Controlled by symptomatic measures	31	39
Moderate—Program of therapy modified	14	18
Severe—Drug therapy discontinued	1	1
Relationship to Lot:		
Lot A (47 Pts. received Lot A)	16	34
Lot B (33 Pts. received Lot B)	30	91
Pain	32	40
Mild	25	31
Moderate	7	9
Severe	0	0
Lot A: 28 per cent; Lot B: 58 per cent.		
Fever	21	26
99-100 degrees F.	12	15
100-102 degrees F.	9	11
Greater than 102 degrees F.	0	0
Lot A: 8 per cent; Lot B: 52 per cent.		
Drug Rash and Allergic Phenomena	19	25
Rash and urticaria	14	18
Edema	3	4
Conjunctivitis	2	3
Lot A: 17 per cent; Lot B: 30 per cent.		
Eighth Cranial Nerve	10	13
Vertigo	6	8
Tinnitus	4	5
Hearing impairment	0	0
Miscellaneous:		
Malaise	8	10
Palpitation	7	9
Anorexia	4	5
Nausea	2	3
Headache	3	4
Palmar fibrosis	3	4
Tetany (Ca)	0	0
Hypotension, lethargy (K)	0	0

Fever: Febrile drug reactions varying from 99 to 102 degrees occurred in one-fourth of the entire series. Without exception, the temperature elevation occurred with the first dose of viomycin and reduction of the dose to one gram every third day in nine patients alleviated this reaction. Fever occurred six times more frequently with Lot B. It is interesting to note that four patients tolerated two grams of Lot A viomycin when a similar dose of Lot B persistently provoked drug fever.

Drug rash and related phenomena: The incidence of maculopapular eruption, urticaria, and edema occurred more frequently in patients who had previously been febrile. The allergic phenomena appeared in 25 per cent of the patients who received viomycin and were prone to occur during the first 60 days. Urticaria was the most common side reaction in this group, and was characterized by: (a) generalized pruritis with typical wheals, (b) rapid appearance following a given dose—occasionally within minutes following administration, (c) prompt response to antihistaminics, (d) inconstant and not reproducible, with a subsequent dose of the same lot, and (e) not correlated with the degree of eosinophilia. Allergy was twice as frequent with Lot B. Persistent rash did not occur in this series but three patients complained of recurrent edema of the fingers for periods ranging from 45 to 60 days. Conjunctivitis was noted in two patients.

The only patient who required discontinuance of drug therapy developed sublingual edema associated with difficulty in swallowing and hoarseness after four weeks of viomycin and PAS. This acute episode simulated angioneurotic edema and responded rapidly to epinephrine. Three episodes of urticaria had preceded this major complication, and it was deemed unwise to continue viomycin therapy. Subsequently the patient tolerated PAS combined with streptomycin.

Three patients gave a history of seasonal asthma, but no exacerbations were encountered during viomycin therapy.

Eighth cranial nerve: Subjective symptoms of vertigo or tinnitus occurred during the latter part of therapy in 10 patients and disappeared after drug treatment was completed. The incidence of vertigo and tinnitus in 36 patients receiving viomycin and streptomycin was 14 per cent as compared with 13 per cent for the entire series and 11 per cent for the group receiving viomycin alone or viomycin with PAS. Objective evidence of eighth cranial nerve damage as measured by serial audiograms and caloric vestibular tests was absent in all patients.

Miscellaneous: Several interesting clinical observations were noted in a small percentage of patients who received viomycin therapy. Twelve per cent of the group experienced malaise every third day concomitant with the administration of viomycin. Anorexia was present in 6 per cent of the series and 3 per cent complained of occasional nausea but none vomited. Seven patients (9 per cent) complained of palpitation every third day associated with the administration of viomycin. History was negative for previous episodes of palpitation or cardiac arrhythmia in all of these patients. Physical examination and electrocardiograms consistently revealed a normal sinus rhythm and no evidence of myocardial damage. Clinical

evidence indicating disturbance of acid-base balance, hypocalcemia, or hypopotassemia was absent.

Three patients developed a curious type of bilateral palmar fibrosis. Physical examination disclosed firmness, tightness of the subcutaneous tissues, and nodulation of the palmar fascia, but the joints of the fingers were not involved. At no time was there evidence of local edema, redness, heat, or pain. All three cases occurred after 60 days of viomycin and partially subsided after completion of therapy. Perhaps the development of this unusual phenomenon was merely coincidental with the administration of viomycin.

Laboratory toxicity: One or more abnormal laboratory determinations were encountered in all patients during drug therapy (Table III).

TABLE III

LABORATORY TOXICITY DURING INTERMITTENT VIOMYCIN THERAPY

	No.	Pct.
RENAL:		
Albuminuria	58	73
Trace to 1 plus	57	71
2 plus	1	1
Persistent during therapy	3	4
Cylindruria	65	81
Occasionally to 3-5/Lpf.	65	81
Greater than 3-5/Lpf.	0	0
Persistent during therapy	2	3
Decreased Fishberg concentration test	0	0
Decreased 15 minute PSP excretion	0	0
Urea clearance:		
Normal clearance	61	78
No change	11	14
Decrease clearance	6	8
Increased bloor urea nitrogen	0	0
ELECTROLYTES:		
Minor decrease in serum K, Ca, Na, or plasma CO_2 combining power	48	60
Major decrease in serum K, Ca, Na, or plasma CO_2 combining power	0	0
HEMOPOIETIC:		
Anemia, leukopenia, leukocytosis	0	0
Eosinophilia: 5-15 per cent of total WBC	68	85
16-25 per cent of total WBC	56	70
26-36 per cent of total WBC	18	23
HEPATIC:		
Abnormal BSP retention or cephalin flocculation test	0	0
EIGHTH CRANIAL NERVE:		
Abnormal audiogram or caloric vestibular test	0	0

Renal: The incidence of albuminuria and cylindruria was 73 and 81 per cent respectively. However, most patients showed only one to three abnormal urinalyses out of a series of 10 performed during 120 days of drug therapy. If six or more of the urine specimens revealed albumin or casts, renal toxicity was considered "persistent during therapy." By this criterion, persistent albuminuria was noted in three patients and persistent cylindruria in two. At no time did the degree of abluminuria exceed two plus and in most instances it was limited to a trace. Cylindruria did not exceed three to five casts per low power field. The appearance of albuminuria and cylindruria was not related to the lot of viomycin employed or to the duration of therapy. The blood urea nitrogen remained within normal limits in all patients throughout the entire period of study.

Renal function remained intact as measured by the ability of the kidney to concentrate urine to a specific gravity of 1.024 and to excrete 20 per cent or more phenolsulphalein dye in 15 minutes. Ninety-two per cent of the series disclosed no change in urea clearance or remained within normal limits when evaluated after 120 days of therapy. The remainder (8 per cent) manifested significant decrease in urea clearance for at least two months after completing therapy.

Electrolytes: Consistent with the absence of clinical manifestations only minor changes in the blood electrolyte pattern were noted. Serum potassium levels between 3.5 and 4.0 mEq/liter were the most frequently encountered electrolyte disturbance. Electrocardiograms occasionally revealed slight changes in the T waves and ST segments. The only supplemental electrolyte therapy employed was potassium chloride for brief intervals. In a few instances serum calcium values between 8.5 and 9.0 milligrams per cent were observed.

Hemopoietic: There were no disturbances in hemoglobin, red blood cell count, or total white blood cell count during the period of viomycin administration. A high incidence of eosinophilia ranging from five to 38 per cent of the total white count was noted. On at least one occasion during therapy approximately one-half of the patients showed 20 per cent and one-fifth over 25 per cent eosinophilia. The presence of eosinophilia could not be correlated with the lot of viomycin or with clinical allergic phenomena.

Other: Liver function studies remained within normal limits in all patients. Audiograms and caloric vestibular tests revealed no evidence of eighth cranial nerve damage.

Bacteriologic response: Sputum conversion and drug sensitivity studies are presented in Table IV. Sputa from eight (36 per cent) of the patients receiving viomycin alone, 17 (47 per cent) of the patients receiving viomycin and streptomycin, and 10 (48 per cent) of those receiving viomycin and PAS were negative by culture at the completion of treatment.

Cultures showing growth in concentrations of 10 micrograms of streptomycin or PAS per milliliter equal to that of the control have arbitrarily been defined as resistant. Prior to viomycin therapy cultures from all patients were sensitive to six or fewer micrograms of the drug per milliliter.

Following the intramuscular administration of one gram of viomycin, plasma concentrations readily exceeded 25 micrograms per milliliter for several hours (Table V). Because an increase in resistance of at least four-fold must occur before growth is inhibited by 25 micrograms of viomycin per milliliter, this value has been selected as the criterion for resistance in this study.

No instance of drug resistance was encountered prior to therapy. Sputa from 44 patients were positive on culture after 120 days of therapy, and only one yielded organisms completely resistant to 25 micrograms of viomycin per milliliter. This exception was one of the 14 patients positive on completion of the regimen employing viomycin alone. Thus the incidence of organisms resistant to viomycin was 7 per cent of the patients yielding positive cultures or 4.5 per cent of the entire series that received intermittent viomycin alone. No viomycin resistance was encountered in the combined regimens.

One of the 36 patients who received viomycin and streptomycin yielded organisms which were completely resistant to 10 micrograms of strepto-

TABLE IV

BACTERIOLOGIC EVALUATION AFTER 120 DAYS OF INTERMITTENT VIOMYCIN THERAPY

REGIMEN	VM Q3	VM Q3 SM Q3	VM Q3 PAS QD
Number of Patients	22	36	21
Negative	8 (36%)	17 (47%)	10 (48%)
Positive	14	19	11
Sensitive to 25 mcg VM/ml	13	19	11
Resistant to 25 mcg VM/ml	1*	0	0
Sensitive to 10 mcg SM/ml		18	
Resistant to 10 mcg SM/ml		1**	
Sensitive to 10 mcg PAS/ml			9
Resistant to 10 mcg PAS/ml			2***

*7 per cent of 14 positive patients or 4.5 per cent of 22 patients.
**5.3 per cent of 19 positive patients or 2.7 per cent of 36 patients.
***18.5 per cent of 18 positive patients or 9.5 per cent of 21 patients.
Resistance was transient in all cases in this study.

TABLE V

AVERAGE PLASMA CONCENTRATION OF VIOMYCIN FOLLOWING SINGLE INTRAMUSCULAR DOSES (micrograms/milliliter)

DOSE	NO. PTS.	*Time in Hours* 0	1	2	4	8
0.5 Gm	10	0	26.5	28.3	16.8	5.2
1.0 Gm	10	0	87.0	68.1	35.3	12.8

mycin per milliliter. This is an incidence of 5.3 per cent of those positive on completion of therapy or 2.7 per cent of this group. Two months after completion of drug treatment this patient yielded cultures completely sensitive to streptomycin.

Transitory resistance to 10 micrograms of PAS per milliliter appeared in two instances during the fourth month of viomycin-PAS therapy, but disappeared within three months after drug was discontinued. The incidence of transitory resistance was 18 per cent of those positive on completion of therapy or 9.5 per cent of the group.

Discussion

A precise evaluation of any chemotherapeutic agent in a disease as protracted and often unpredictable as pulmonary tuberculosis is a difficult and sometimes misleading task. This viomycin study admittedly is limited but from it, and from previous work at this hospital,[9,10] certain concepts appear justified (Table VI).

Intermittent viomycin alone resulted in a favorable, though slight, response in the majority of patients with advanced pulmonary tuberculosis. It is readily apparent that, gram for gram, viomycin did not equal the clinically established effectiveness of streptomycin in this disease. Viomycin in dosage of two grams every third day approximated the therapeutic efficacy of 12 grams of PAS daily.

The combination of viomycin and PAS was more beneficial than either alone, both from the viewpoint of therapeutic response and the development of bacterial resistance. No resistance to viomycin was noted in this

TABLE VI

COMPARISON OF INTERMITTENT VIOMYCIN WITH OTHER DRUG REGIMENS

REGIMEN	Number Patients	X-Ray Improvement (Percentage) All Degrees	X-Ray Improvement (Percentage) Moderate & Marked	Bacteriologic Response (Percentage) Negative	Bacteriologic Response (Percentage) Resistant*	
VM 2 GM Q3	22	77	9	36		7
PAS 12 GM QD	25	76	8	28		33
SM 2 GM Q3	97	71	28	37		33
VM 2 GM Q3 plus PAS 12 GM QD	21	95	19	48	VM PAS	0 18
VM 2 GM Q3 plus SM 2 GM Q3	36	83	39	50	VM SM	0 5
SM 2 GM Q3 plus PAS 12 GM QD	95	89	48	67	SM PAS	0 0
SM 2 GM Q3 plus PAS 12 GM Q3	103	96	42	49	SM PAS	30 0

*Per cent based on number of patients yielding positive cultures on completion of therapy.

combined series. In the case of two patients whose sputa yielded organisms resistant to 10 micrograms of PAS per milliliter subsequent studies showed that this phenomenon was transitory.

Similarly, the combination of intermittent viomycin and intermittent streptomycin was considerably more effective than either agent alone. Intermittent viomycin-streptomycin was superior to the intermittent viomycin-daily PAS regimen and approximated our experience with intermittent streptomycin and daily PAS. The single instance of resistance to 10 micrograms of streptomycin per milliliter in this series implies that viomycin was capable of modifying the predicted incidence of resistance to streptomycin. When combined with streptomycin, intermittent viomycin was more effective than intermittent PAS in delaying the emergence of streptomycin resistance, but less effective than daily PAS.

Intermittent viomycin, two grams every third day, provoked a high incidence of mild untoward reactions. The frequency of significant pain at the site of intramuscular injection (40 per cent), fever (26 per cent), and drug rash (18 per cent) presented many difficulties in maintaining patient acceptance of this new drug. For this reason prolonged administration beyond 120 days was impractical in the few instances in which it was attempted. Correlation of adverse drug reactions with the lots employed suggests that impurities may have accounted for some of the clinical toxicity noted.

Mild renal irritation was evidenced in the majority of patients by occasional cylindruria and slight albuminuria, which disappeared after termination of drug therapy. Disturbances of renal function, as measured by the 15 minute PSP excretion and Fishberg urine concentration tests, and nitrogen retention were not observed. However, six patients had diminished urea clearance. The precise significance of this, in the absence of other abnormality, could not be determined. We believe that the renal toxicity from intermittent viomycin was minimal in extent and transient in duration in the majority of patients.

In striking contrast to the serious eighth cranial nerve dysfunction and serum electrolyte disturbance reported by others with daily viomycin, intermittent therapy produced only minor toxic manifestations. However, pre-existing renal disease should probably remain a relative contraindication to viomycin therapy.

SUMMARY

An evaluation of 80 patients with pulmonary tuberculosis who received intermittent viomycin, two grams every third day, singly or combined with intermittent streptomycin or daily para-aminosalicylic acid for 120 days suggests that this agent is capable of exerting a favorable effect on the clinical course of the disease. The therapeutic effectiveness of this drug was considerably less than streptomycin, but approximated that of PAS. Viomycin combined with either streptomycin or para-aminosalicylic acid was superior to any of the drugs employed alone.

The high incidence of clinical and laboratory toxicity which accompanied

intermittent viomycin was predominantly minor, transient, and reversible after termination of therapy. This is in striking contrast to toxicity reported when viomycin is administered daily. It is believed that viomycin is a relatively safe drug when administered intermittently, provided its potential toxicity is appreciated and appropriate clinical and laboratory surveillance is maintained.

RESUMEN

Una evaluación de 80 pacientes con tuberculosis pulmonar que recibieron Viomicina intermitente, dos gramos cada tercer dia sola o combinada con estreptomicina intermitente o ácido paramino salicílico diario por 120 días sugiere que este agente es capaz de ejercer un efecto favorable en el curso clínico de la enfermedad. La efectividad terapéutica de esa droga es considerablemente menor a la de estreptomicina, pero aproximadamente igual a la del PAS. La viomicina empleada combinadamente con la estreptomicina o el ácido paramino salicílico fué superior a cualquiera de las drogas usada sola.

La alta incidencia de toxicidad clínica y de laboratorio que acompañó a la Viomicina fué predominantemente menos transitoria y reversible después de terminada la terapia. Esto produce un significativo contraste con la toxicidad presentada cuando la Viomicina se administra a diario. Se cree que la Viomicina es una droga relativamente segura cuando se aplica intermitentemente, siempre y cuando se aprecie su potencial de toxicidad y se mantenga vigilancia apropiada tanto clínica como de laboratorio.

RESUME

L'étude de 80 malades atteints de tuberculose pulmonaire, et qui ont été traités par la viomycine de façon intermittente, donne l'impression que ce produit est susceptible d'avoir une action favorable sur l'évolution de la maladie. Le traitement a consisté en deux grammes de viomycine tous les trois jours pendant 120 jours, soit à titre isolé, soit combiné avec un traitement intermittent à la streptomycine ou un traitement quotidien par le P.A.S. L'efficacité de la viomycine a semblé infiniment moindre que celle de la streptomycine mais peu différente de celle du P.A.S. La combinaison de viomycine avec la streptomycine ou le P.A.S. s'est montrée supérieure à chacune de ces drogues utilisée isoliment.

Au lieu de la grande fréquence habituelle de la toxicité clinique et biologique de la viomycine administrée quotidiennement, le traitement intermittent ne montre que des complications généralment discrètes, éphémères et disparaissant avec la terminaison du traitement. Les auteurs estiment que la viomycine est une thérapeutique relativement sans danger quand elle est administrée d'une façon intermittent, à condition de savoir apprécier son potential toxique et de maintenir la surveillance clinique et biologique nécessaire.

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Segmental Resection in Tuberculosis*

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The total extirpation of the offending lesion and the preservation of as much normal lung tissue as possible are the major objectives in excisional treatment of pulmonary disease. The increased use of limited resection represents the surgical approach to obtain these desirable objectives. For more than a decade, segmental resection has been accepted as a rational procedure especially in the treatment of bronchiectasis, a disease process which usually has a typical segmental distribution. The acceptance of segmental resection as a rational approach in the surgical treatment of tuberculosis was delayed by the concept that tuberculosis is a disseminated disease, never well confined to segmental boundaries. However, in recent years the exploration of early tuberculous lesions has demonstrated that the major necrotic lesion is frequently confined to one or two segments. In addition, the antimicrobial drugs have come upon the scene and made all surgical procedures much safer in the tuberculous patient. They frequently result in such complete resolution of the disease process that the residual necrotic focus is well contained in a segment, subsegment, or even a smaller unit of the lung. These facts plus the surgeons improved knowledge of the segmental anatomy and increased experience with this surgical procedure has led to rapid expansion in the use of segmental resection in the treatment of tuberculosis.

Numerous reports have appeared during the past few years on the use of this procedure. By and large, the reported results are excellent. However, it is timely to emphasize that such results are secured only when segmental resection is used in a carefully selected group of patients. These are usually in excellent general condition, are in good immunological balance with their disease, and have limited lesions. The surgery is applied at the ideal time under the protection of the antimicrobial drugs in a well coordinated therapeutic program. When segmental resection is used in patients representing failures to other collapse therapy or surgical procedures, or in the presence of extensive disease as a salvage procedure, results are not so happy; in fact, they are poor.

The purpose of this paper is to contrast results in these two groups of patients and to define the place of segmental resection in the surgical treatment of tuberculosis.

This study consists of an analysis of 123 segmental resections performed in the streptomycin era between January, 1947 and January, 1952. During this period, a total of 539 resections were performed in the treatment of

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pulmonary tuberculosis (Table I). Seventy-five of the 123 had only segmental resection. In most instances, this represented the excision of one segment or two adjacent segments. Occasionally, segments from two different lobes were removed. In 48 patients, segmental resection was used in addition to lobectomy. This group consists almost entirely of the combination of upper lobectomy and resection of the superior segment of the lower lobe.

Figure 1 illustrates the increasing utilization of segmental resection with each succeeding year. Whereas in 1947, segmental resection was used in only 4 per cent of the cases; in 1951, the proportion had risen to 33 per cent. In recent years, no other operative procedure has been used with

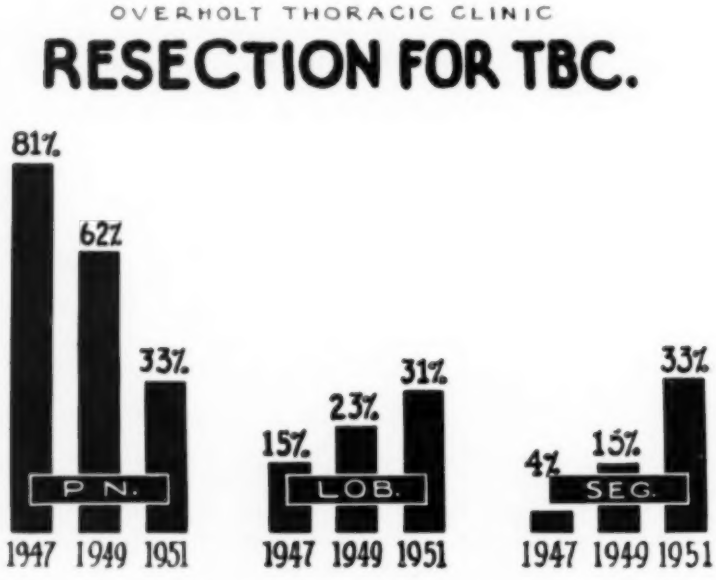

FIGURE 1: Illustrates the comparative use of pneumonectomies, lobectomies, and segmental resections in the past five years. Note the decreasing portion of pneumonectomies and the sharply increasing portion of segmental resections.

TABLE I

RESECTION FOR TUBERCULOSIS

January, 1947 - January, 1952

Total		539
Pneumonectomy	258	
Lobectomy	155	
Segmental	75	
Segmental plus Lobectomy	48	
Wedge	3	

greater frequency in the resectional treatment of pulmonary tuberculosis. If it were not for the considerable number of far advanced patients referred to this clinic from outside sources, the percentage of segmental resections would be even higher.

Plan of Paper and Definition of Terms:

Postoperative statistics will be presented for the entire group of 123 patients. The postoperative period consists of an arbitrary period of 60 days following operation. The follow-up statistics give the status as determined in July, 1951 of the 61 patients operated on prior to January, 1951. Thus, the minimum follow-up time is six months and the maximum four and a half years. Those having only segmental resection and those having segmental resection and lobectomy are considered separately.

Patients are listed as clinically well with negative sputum when that represents the opinion of the physician now caring for them. Because of the wide geographical distribution of our patients, a standard bacteriological evaluation has been impossible. Those classified as "? favorable" are clinically well but have either an intermittently positive sputum or an unstable x-ray lesion. Those classified as "? unfavorable" have active or progressive tuberculosis or are respiratory cripples.

In each table, the patients have been divided into three groups. Those having had previous surgery or collapse therapy procedures (pneumoperitoneum excluded) are designated as "secondary resection." Those having segmental resection as the first surgical procedure are referred to as "primary resection." When primary resection was used within the first year following diagnosis, it is labelled "early primary resection." The reader is reminded that this last group is a subdivision of the "primary resection" group. Thus, the total number of patients in each table is the sum of those in the "secondary" and "primary" treatment groups; whereas, the column headed "early primary resection" represents additional observations on part of the "primary resection" group.

The reason our statistics are presented in groups divided into primary and secondary is that experience has shown that there is an increased morbidity and mortality rate associated with secondary segmental resection. We shall emphasize this fact throughout the paper.

The total number of patients in some of these groups is small and, therefore, the statistics are not significant in themselves. However, the contrast between the primary and secondary resection groups is so definite that we feel the statistics indicate a significant and consistent trend.

Table II gives the postoperative statistics for 75 pure segmental resections performed between January, 1947 and January, 1952. Fifty were primary resections; whereas 25 had previous surgical procedures.

There is a sharp contrast in tuberculous complications in favor of the primary resection group. Tuberculous death rate was low in all groups, but it is significant that there was none in the primary resection group. Nontuberculous deaths occurred just half as frequently in the primary as in the secondary resection groups (4 per cent vs. 8 per cent).

Not only did complications occur more frequently in the secondary group but they were more serious. The one complication in the primary resection series was a wound infection. The four complications in the secondary group consisted of (1) ipsolateral exacerbation, (2) fistula and empyema, (3) fistula, empyema and ipsolateral spread, and (4) fistula, empyema and bilateral spread which resulted in death on the 41st day. The two non-tuberculous deaths in the primary group were due to shock and embolus. In the secondary group, they were both due to pulmonary insufficiency. Both of these patients had had previous thoracoplasty on the operative side. One had contralateral pneumothorax existing at the time of operation. The other had had pneumothorax prior to his thoracoplasty on the same side and his contralateral lung was involved with extensive nodulation. These two patients emphasize the danger of applying even limited resection to patients with marginal respiratory reserves as a result of previous collapse therapy and extensive disease.

We would like to focus the attention of the reader on the 28 patients in the early primary resection group. There was no tuberculous complication, no tuberculous death, and one patient died of postoperative shock. These statistics reflect the results of the early use of segmental resection in a well coordinated plan of treatment.

TABLE II

POSTOPERATIVE STATISTICS

January, 1947 - January, 1952

Segmental Resection Only

TOTAL 75	Secondary Resection 25		Primary Resection 50		Early Primary Resection 28	
	No.	Pct.	No.	Pct.	No.	Pct.
Tuberculous Complications	4	16	1	2	0	0
Tuberculous Deaths	1	4	0	0	0	0
Non-Tuberculous Deaths	2	8	2	4	1	3.6
Total Deaths	3	12	2	4	1	3.6

TABLE III

POSTOPERATIVE STATISTICS

January, 1947 - January, 1952

Lobectomy Plus Segmental Resection

TOTAL 48	Secondary Resection 28		Primary Resection 20		Early Primary Resection 8	
	No.	Pct.	No.	Pct.	No.	Pct.
Tuberculous Complications	3	10.7	0	0	0	0
Tuberculous Deaths	0	0	0	0	0	0
Non-tuberculous Deaths	3	10.7	1	5	0	0
Total Deaths	3	10.7	1	5	0	0

Table III gives the postoperative statistics for the 48 patients subjected to both lobectomy and segmental resection. Only 20 of these had primary resection and in only eight of these was it performed in the first year of the disease. This table is self-explanatory and shows again that the primary use of resection leads to reduced morbidity and mortality rates. The most significant part is the contrast in tuberculous complications between the two groups—10.7 per cent as compared with 0 per cent. Tuberculous complications in the secondary resections consisted of fistula and empyema in two and tuberculous empyema and wound infection in one.

There was no tuberculous death in either group. The non-tuberculous deaths in the secondary resection series were caused by pulmonary embolus, hemorrhage from a contralateral cavity and pulmonary insufficiency. The one death in the primary group was due to pulmonary embolus.

Table IV summarizes the late results of the group of 36 patients who had segmental resection between January, 1947 and January, 1951. As previously noted, the proportion of postoperative deaths in the secondary resection group considerably exceeds that in the primary group (20 per cent to 3.8 per cent). Likewise, the danger of late death is much more in the secondary resection group (20 per cent) than the primary resection group where there was none. One of these late deaths followed a subsequent resection; the patient had had a right upper lobectomy elsewhere followed by empyema and bronchopleural fistula. The superior segment of the lower lobe was removed but again was followed by empyema and bronchopleural fistula. At a third operation, pneumonectomy was completed but death due to shock followed. The other late death occurred 18 months postoperatively due to progressive ipsolateral disease.

The marked difference in the end results, when segmental resection is used as a primary rather than a secondary procedure, is striking. Of the 10 secondary resections, four are dead; one is classified as unfavorable; and only five are clinically well with negative sputum. By contrast, 24 of the 26 primary resections are completely well. Special attention is called to the 16 patients in the early primary resection group. With the exception

TABLE IV

SEGMENTAL RESECTION

January, 1947 - January, 1951

Results (July, 1951)

TOTAL 36	Secondary Resection 10		Primary Resection 26		Early Primary Resection 16	
	No.	Pct.	No.	Pct.	No.	Pct.
Postoperative Deaths	2	20	1	3.8	1	6.3
Late Deaths	2	20	0	0	0	0
Clinically Well and Negative	5	50	24	92	15	94
? Favorable	0	0	0	0	0	0
? Unfavorable	1	10	1	3.8	0	0

of one patient who died of operative shock, all patients are living and well.

In spite of the ultimate good result in the primary group, three patients had late tuberculous complications—(1) ipsolateral exacerbation and contralateral spread, (2) ipsolateral exacerbation, and (3) wound infection. None of these three patients had adequate antimicrobial therapy according to modern standards.

Table V contrasts the late results of secondary and primary resection in 25 patients who had both lobectomy and segmental resection. There is no significant contrast as far as postoperative and late deaths go. The single late death in the secondary group came from hemorrhage into a complicating empyema. Again, there is an appreciable contrast between the 87.5 per cent well and negative in the primary resection group and the 59 per cent well and negative in the secondary group. Furthermore, the eventual outcome of a number of the secondary resection group is in doubt while none in the primary group are classed in the doubtful group—(? favorable and ? unfavorable). There were late complications in two cases in each group again indicating that the battle is not won by successfully passing the postoperative period. Two patients in the secondary group had contralateral exacerbation, and two in the primary group had wound infections. Note that the type of complication is more serious in the secondary group.

TABLE V
LOBECTOMY PLUS SEGMENTAL
January, 1947 - January, 1951
Results (July, 1951)

TOTAL 25	Secondary Resection 17		Primary Resection 8		Early Primary Resection 3	
	No.	Pct.	No.	Pct.	No.	Pct.
Postoperative Deaths	1	6	1	12.5	0	0
Late Deaths	1	6	0	0	0	0
Clinically Well and Negative	10	50	7	87.5	3	100
? Favorable	4	24	0	0	0	0
? Unfavorable	1	6	0	0	0	0

TABLE VI
INFLUENCE OF PRIMARY AND EARLY PRIMARY RESECTION ON FOLLOW-UP STATISTICS*

TOTAL	Secondary Resection	Primary Resection	Early Primary Resection
Pneumonectomy	71	71	80
Lobectomy	72	86	85
Lobectomy and Segmental	59	87.5	100
Segmental	50	92	94

*Percentages record the proportion of each group clinically well with negative sputum.

Comparison of the end results (as judged by the percentage of patients living and well with negative sputum) is made in Table VI for pneumonectomy, lobectomy, segmental resection plus lobectomy, and segmental resection alone. It is striking that in all categories early primary resection leads to the best end results. The results of primary resection are consistently better than secondary resection except in pneumonectomy where there is no difference. In lobectomy, there is an appreciable difference, but in segmental resection both with and without lobectomy primary resection proves much superior. The end results of secondary resection are unsatisfactory in these groups, and indeed inferior to results with either pneumonectomy or lobectomy.

Discussion

Results following primary segmental resection are excellent with 92 per cent of the original treatment group and 96 per cent of the living patients classified as clinically well with negative sputum. However, these results are not and should not be interpreted as a measure of the safety and effectiveness of the operative procedure alone. They are secured only when segmental resection is used in a very select group of patients who have the initial or residual necrotic lesions well contained within segmental boundaries and have their operation applied as the primary surgical procedure. These patients are in good general condition and are in immunological balance with their disease. They also represent by and large a group which has been treated intelligently in a well coordinated program consisting of bed rest and the antimicrobial drugs. Excellent results in such an ideal group of patients should be expected. In fact, they are obligatory since a high percentage can be treated very successfully by other measures.

In contrast to the primary group, results with the use of segmental resection as a secondary procedure are poor. Our statistics indicate that segmental resection under certain circumstances can be the most dangerous of all resections. When segmental planes are obliterated and adjacent segments contain nodulation and emphysema, or when the segment being removed contains the residual cavity but there is widespread nodulation throughout the remainder of the lung tissue, results will be poor. When preservation of function nad lung volume is a vital factor in a case with very marginal respiratory reserve, the surgeon may be justified in using segmental resection in the face of such adverse conditions. However, it is usually the better part of wisdom to use another approach to such problems. The surgeon must learn to think clearly about just how much function the use of segmental resection will save in a given case (e.g. preserving the anterior segment of the right upper lobe) and weigh this against the risk of complications. An ounce of function is never worth a pound of risk. In our experience, under certain conditions, lobectomy is a much safer operation than segmental resection and frequently thoracoplasty is safer than either of them.

The primary use of resection is a very important factor in determining

the end results with resection, especially when applied early in the course of the disease. Of the 346 resections in our follow-up series, 87 had early primary resection. Of this group, 90.8 per cent are living, six months to four and a half years after operation, and 94 per cent of the living patients are completely well. These results compare favorably with the segmental series. Yet an analysis of the 87 cases reveals that 41 were pneumonectomies, 27 lobectomies, three lobectomy plus segmental resection, and only 16 were segmental resections. This would seem to indicate that the use of early primary resection is of more importance than the type of operation. Most segmental resection series are heavily weighted with such cases. These statistics also emphasize the fact that good results can be expected with any type of resection if the following important criteria exist:

1) Adequate respiratory reserve.
2) The lesion is well confined within the limits of the unit of lung to be excised.
3) Resection is the primary surgical approach to the problem.
4) Resection is applied as soon as ideal conditions have been secured with bed rest and antimicrobial drugs.

In recent years more and more reports have appeared on very limited pulmonary resections applied to such small lesions. These do not in any way represent the surgical treatment of the tuberculous patient group as a whole. They represent a very select group of patients in which the factors discussed above play a major role in determining the end results. The excellent statistics with such procedures justify their use. However, it is very important that we orient such procedures in the total picture of the surgical treatment of tuberculosis. Because of the type of case contained in such groups, the statistics cannot be compared with other surgical pro-

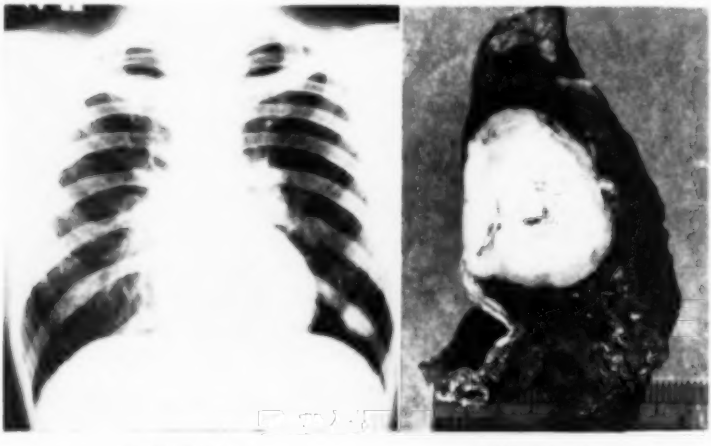

FIGURE 2a FIGURE 2b

Figures 2a and 2b: Oval lesion at left base, removed by segmental resection and found to be tuberculoma.

cedures which are applied in a greater percentage of patients secondarily to more extensive lesions and in patients in poorer general condition.

Case Reports

The following three cases are presented in brief to illustrate problems in the treatment of tuberculosis for which we have applied segmental resection.

R.S.: A 29 year old male was found to have an oval density by routine chest x-ray film (Figure 2a) at the left base. The lesion was known to have enlarged slightly since discovery two years before. Except for slight cough and sputum, he was well and preoperative study failed to make an etiological diagnosis. The chest was explored and the lateral basal segment of the left lower lobe removed. Immediate pathological examination showed it to be a tuberculoma (Figure 2b). The chest was closed and he has been well in the subsequent three and a half years.

Note: This illustrates a "tuberculoma" removed in part because preoperative study could not eliminate the possibility of tumor. Such enlarging "tuberculomata" are in themselves a potential hazard and should be removed.

W.K.: A 34 year old white male had been treated for tuberculosis for six months with streptomycin and PAS. The sputum remained positive. The only finding by chest x-ray film was a localized cavity in the posterior segment of the left upper lobe (Figure 3a). This segment was removed (Figure 3b) and the patient has been well and sputum negative for 17 months.

Note: This illustrates a well localized lesion which might have healed on prolonged treatment of other kinds but would have remained a potential hazard.

S.L.: A 25 year old male had had bilateral tuberculosis for five years and had been treated by pneumothorax on both sides. Several courses of streptomycin had been given. He was left with extensive bilateral pulmonary damage, positive sputum, evidence of endobronchial tuberculosis on the right, and cavities in the deformed right upper lobe and superior segment of the lower lobe (Figure 4). A right upper lobectomy and resection of the superior segment and one basal segment of the right lower lobe was done. The postoperative course was complicated

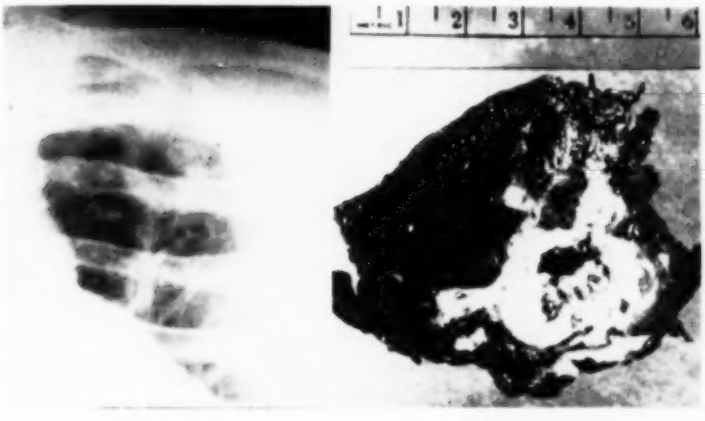

FIGURE 3a FIGURE 3b

Figures 3a and 3b: Cavity in the posterior segment of the left upper lobe removed by segmental resection.

and empyema and bronchopleural fistula developed. These led to further complications and death.

Note: Whenever forced by poor function and widely scattered disease to attempt salvage by segmental resection, one cannot expect a high percentage of cures.

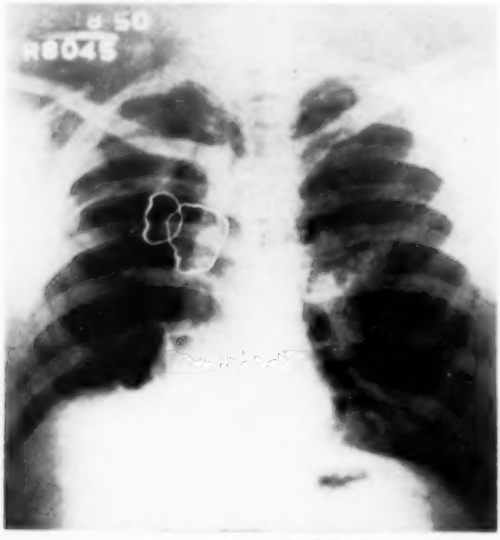

FIGURE 4: Bilateral longstanding tuberculosis. The two cavities in the right upper lobe and the superior segment of the lower lobe are retouched. Segmental resection in such complicated cases is associated with high morbidity and mortality.

SUMMARY

1) Segmental resection is being used more frequently and now represents one of the most commonly used surgical procedures in the treatment of pulmonary tuberculosis.

2) Excellent results are secured with segmental resection when it is used as the primary procedure in cases with lesions well limited to the segment or segments being resected.

3) Poor results are encountered when segmental resection is used in patients with widespread disease or when used as a secondary procedure.

4) The excellent results with segmental resection are a reflection of the limited disease being treated, the excellent condition of the patients, and the fact that the surgical procedure has been used primarily.

RESUMEN

1) La resección segmentaria está siendo usada mas frecuentemente y representa ahora uno de los procedimientos quirúrgicos mas comunes para el tratamiento de la tuberculosis pulmonar.

2) Se aseguran excelentes resultados con la resección segmentaria cuando se usa como procedimiento primario en casos con lesiones bien delimitadas al segmento o segmentos que se resecan.

3) Resultados pobres se obtienen con la resección segmentaria cuando se usa en pacientes con la enfermedad muy avanzada o se usa como procedimiento secundario.

4) Los excelentes resultados obtenidos con la resección segmentaria son un reflejo del tratamiento cuando la enfermedad limitada que es tratada, la excelente condición de los pacientes y el hecho de que el procedimiento quirúrgico fué usado primariamente.

RESUME

1) La résection segmentaire est utilisée plus fréquemment et représente maintenant un des procédés chirurgicaux les plus communs dans le traitement de la tuberculose pulmonaire.

2) Les résultats sont excellents quand cette intervention est utilisée d'emblée dans les cas de lésions bien limitées aux segments uniques ou multiples qui ont été l'objet de l'exérèse.

3) Les résultats sont médiocres quand on utilise l'exérèse segmentaire chez des malades atteints de tuberculose étendue ou lorsque cette technique est utilisée comme procédé secondaire.

4) Lorsqu'on obtient des résultats excellents, ceci correspond aux cas de lésions limitées où l'état général du malade est parfait, et pour lequel l'intervention chirurgicale a été faite d'emblée.

A Critique of the International Nomenclature on Bronchopulmonary Segments*

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In the summer of 1949, the International Congress of Oto-Rhino-Laryngology met in London. Anticipating the opportunity presented by the bringing together of men from different countries who were interested in the bronchial tree, Professor Huizinga of Groningen proposed the formation of an international committee of 15 (drawn from those present in London) to explore the possibility of establishing a common nomenclature. It was also recommended that the current subcommittee report of the Thoracic Society of Great Britain be accepted as a convenient basis for discussion.† Agreement was reached after four hours discussion, and the report of this unofficial international committee was subsequently adopted both by the Congress (July, 1949) and by the Thoracic Society (February, 1950).††

The scheme as finally approved is shown in Figure 1. Obviously this marks a great step forward. At the risk of minimizing an accomplishment which was very substantial, the writer ventures to discuss certain points at issue.

First, it will be noted that the bronchi are numbered, which is a great advantage. The order of numbering corresponds to that adopted by the writer (Surgery, 1945), except that Nos. 2 and 3 are interchanged. Presumably the reason for the latter is that in bronchography the PA appearances favor placing the posterior bronchus second on the list. (The lateral view does not favor this order). Also, on the left side, the apical and posterior bronchi arise from a common stem. For the anatomist and the surgeon, however, the apical and anterior bronchi are the first ones encountered at the hilum; the posterior bronchus and its vessels are deeply hidden. Therefore numbering the posterior bronchus of the upper lobe last (B-3) has seemed to be a more natural order.§

Secondly, a most important issue is the omission of B-7 from the left lung. This was omitted partly because the area is rarely the site of lesions and partly on grounds of comparative anatomy. In quadrupeds, for instance, the cardiac lobe is found only in the right lung. But Ewart disposed of such arguments in 1889 by pointing out that in man the differing shape of the thorax and differing position of the heart necessitate a new ap-

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†The members of this subcommittee were Mr. V. E. Negus, Mr. R. C. Brock, Dr. A. F. Foster-Carter and the late Professor A. B. Appleton.

††A complete account of the report has been published by Brock in Thorax, 1950, and also discussed in the book by Huizinga and Smelt, 1949.

§Apparently, the committee gave no thought as to whether their enumeration of bronchi was favorable or unfavorable to the better presentation of the pulmonary vessels. Yet in devising a permanent terminology, should not the lung be considered as a whole?

proach to the problem. He recognized a retro-cardiac (medial basal) district in the left lung. Even Narath, the Dutch surgeon whose monumental study of mammalian lungs has never been surpassed, recognized a left cardiac bronchus in the human lung, even while insisting that human

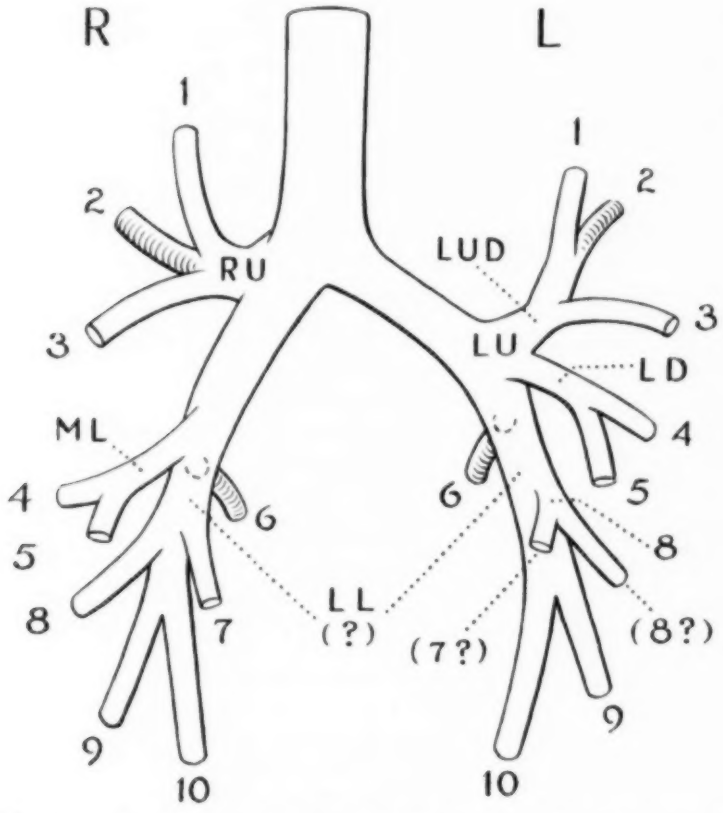

FIGURE 1: Diagram of bronchial tree illustrating terminology recommended by unofficial international committee (1949). RU, LU, right and left upper lobe bronchi; ML, middle lobe bronchus; LUD, LD, left upper division and lingular (lower) division; LL, lower lobe bronchi. Bronchi and segments:

Right	*Left*
1. apical	1. } apico-posterior
2. posterior	2. }
3. anterior	3. anterior
4. lateral	4. superior
5. medial	5. inferior
6. apical	6. apical
7. medial basal (cardiac)	7. (omitted)
8. anterior basal	8. anterior basal
9. lateral basal	9. lateral basal
10. posterior basal	10. posterior basal

Note: (7?) and (8?) represent opposing interpretations. (See text beginning "Secondly").

and quadruped patterns are homologous. So, also, did such other adherents to the stem bronchus doctrine as Lucien and Weber, 1936—who made the first detailed modern study of the "cardiac territory."

Anatomically, the evidence is strongly in favor of a left cardiac region. If one looks at the diaphragmatic surface of the lungs* it is obvious that Segment 7 of the left lung is equal in size to that of the right; it has merely been displaced laterally by the heart. Another reason is that the medial basal component is more stable than the one whose name has been given to the whole stem. For the anterior basal portion is defective in origin or distribution (or both) in 27 per cent of specimens.** Finally, in 10 per cent, the medial basal arises separately from the left lower lobe bronchus in a position comparable to that of the right medial basal. Surely this is of practical importance in identifying bronchograms. Accordingly, it is strongly recommended that a medial basal zone be recognized on the left side. Who knows when it may not become clinically significant?

Thirdly, another decision which might be considered anatomically unsound is the naming of a fourth (or lateral) segmental bronchus in the right upper lobe. Granted that it represents merely an anomalous arrangement occurring in some 10 per cent of specimens—our figures reach 16 per cent—one may question the advisability of giving it a name which perpetuates the error of those who originally described the right upper lobe as consisting of four segments. If it is to be named at all—in so brief a terminology—why not give it a name which tells what it is—namely the lower ramus of the posterior segment (our B-3b).†

Fourthly, the applications of the term "apical" to the superior segments of the lower lobes (as originally used by Glass) would seem to violate the third principle laid down by the French Committee—namely that a term should "conform to the classical descriptive anatomy." For centuries anatomists have recognized only one apex to a lung. Every one understands what part of the lung is meant by that term. The reason given—namely that the term "subapical" is more euphonious than the term "subsuperior"—seems trivial beside the disadvantage of giving the same name to such different parts of the lung. Another argument advanced is that "superior" is the name given to the fourth segment of the left upper lobe, but in practice this is always called the "superior lingular," and in the writer's opinion should be so named, officially.

Fifthly, no decision was reached about naming that portion of the right bronchus which lies between the upper lobe and middle lobe bronchi. Some wished to call it the "right stem bronchus" and others the "right main bronchus." The Thoracic Society finally adopted a modified version, naming the trunk which extends from the bifurcation to the middle lobe trunk, "the right main bronchus." This was subdivided into upper and lower parts,

*Cf. Fig. 10 in article entitled "A Synthesis of the Prevailing Patterns of the Bronchopulmonary Segments in the Light of Their Variations," *Dis. of Chest*, 15:657-668, 1949.

**Berg, Boyden and Smith, *J. Thoracic Surg.*, 18:216-236, 1949.

†See discussion of quadrivial pattern on page 36 of article by Boyden and Scannell, *Am. Jour. Anat.*, 82:27-74, 1948.

the latter corresponding to the truncus intermedius of Ewart. (Presumably the term "left main bronchus" would be applied to the unbranched portion of the left bronchus).

In considering these alternate terms it seems to the writer that nothing has been gained in dropping the term "stem bronchus." Embryologically, there is a stem bronchus. The question is how far does it extend inferiorly? The same problem arises about the limit of a "main bronchus." In either case it has to be defined arbitrarily.

Sixthly, the use of the term "lower lobe bronchus" may be questioned. According to Huizinga's diagram (which supposedly incorporates the conclusions of this international committee) the name is applied to the trunk which lies *below* B-6. But surely B-6 is the first branch of the lower lobe bronchus. Would it not be more logical therefore, to consider the lower lobe bronchus as dividing into superior and basal parts or trunks?

Seventhly, there is no mention of the subsuperior bronchus. In the right lung this was found to be present in 61 per cent of 100 specimens (Ferry and Boyden, 1951).

Finally, in view of these considerations may it not be advisable to hold to the Jackson-Huber terminology until such a time as an official international committee can deal with these problems. In this connection it may be noted that three standard textbooks of Anatomy—the latest American editions of Cunningham, Gray and the impending Morris—have all adopted the Jackson-Huber terminology.

Some Basic Biologic Effects of Cortisone as Related to Pulmonary Disease*

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ACTH and cortisone have now been used in a wide variety of pulmonary conditions such as acute pneumonia, tuberculosis, chronic granulomata, and bronchial asthma. Varying results have been obtained. In some of these conditions there has been little or no effect, in others a distinctly deleterious effect and in still others there has been some benefit at least for a short time. On the other hand, the use of cortisone for non-pulmonary conditions has occasionally resulted in a development of certain serious pulmonary complications. Sufficient basic experimental investigations have been reported so that it is now possible to understand the means whereby ACTH and cortisone produce both beneficial and harmful therapeutic effects. These studies relate in particular to the effect of cortisone on the acute inflammatory process, on the formation of granulation tissue and on the allergic and immune mechanisms.

One of the most significant effects of ACTH and cortisone is to alter the acute inflammatory process.[1-5] This alteration is both quantitative and qualitative in its characteristics. Numerous studies, both experimental and clinical, indicate that there is a marked suppression of the acute inflammatory responses to almost all forms of noxious agents whether they be physical, chemical, viral, bacterial, or of a foreign body nature. This suppression is characterized by a marked decrease in the number of leucocytes, in the quantity of fibrin, and in the amount of edema fluid at the site of local injury. The inflammatory response is distinctly less hyperemic and margination of leucocytes is markedly reduced. Polymorphonuclear leucocytes are considerably less phagocytic.[6] Not only are there less mononuclear cells present but those that are present are probably not functioning properly. For these reasons the site of injury is inadequately localized and in the late stages of the acute inflammatory process necrosis may be present in adjacent areas which otherwise would not have been involved.[3] Although late necrosis has been seen, some observers had reported less necrosis in the early phases of acute inflammation. Some studies have also indicated a greater tendency exists for blood stream invasion of bacterial infections.[7] The mechanisms through which ACTH and cortisone suppress all elements of the acute inflammatory process are not as yet

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completely defined. However, various experimental studies and those in particular utilizing the rabbit ear chamber technic have shown that there is a marked increase in vascular tone with considerably less capillary permeability present.[8] This in turn would tend to prevent the migration and exudation of those cellular, chemical and fluid elements which make up the acute inflammatory exudate. Some believe that this decrease in vascular permeability is caused by a neutralization of leucotaxine by the cortisone.[9] Others believe that the initial inhibition of necrosis of tissue by cortisone prevents the trigger mechanism of acute inflammation from being set into motion. The degree of suppression of the acute inflammatory process appears to be directly related to the dosage of ACTH and cortisone employed.[10] Even with large doses of cortisone, the acute inflammatory process may not be suppressed if the injury responsible for the inflammation is extensive or extremely virulent. It appears that a balance between the dose of cortisone and the virulence and dosage of the noxious agent will determine the extent of the change in the acute inflammatory process. It has also been demonstrated that a dose of cortisone as low as 0.00025 mg. is sufficient to produce a significant eosinophile depression in adrenalectomized mice.[11] On the other hand, 0.25 mg. of cortisone is required to produce a significant inhibition of the inflammatory response in mice produced by a moderate chemical injury.[10] Thus it is important to note that there is a wide difference in the magnitude of the cortisone dose required for an adequate eosinophile response and for the suppression of inflammation. This is of interest because circulating eosinophile responses are used by some as a measure of therapeutic activity.

Another important effect of cortisone is its influence on the repair process.[12,13] It has been demonstrated in both experimental and clinical studies that these hormones can significantly inhibit wound healing and granulation tissue formation. As with the case of inflammation the effect on granulation tissue is both quantitative and qualitative. Not only are the number of fibroblasts reduced but those that are present present a somewhat atypical appearance. The granulation tissue is less vascular, with few new proliferating capillary buds present. The intercellular ground substance is scant and does not stain in its characteristic way with the metachromatic stains. The granulation tissue is less compact and does not proceed to collagenization with the same dispatch as in the untreated animal. Dosage levels of cortisone in the experimental animal required for the inhibition of granulation tissue formation are comparable to the dosage levels required for the suppression of the acute inflammatory process and the larger dose the greater the degree of suppression. The exact mechanism whereby these hormones inhibit the formation of fibrous tissue is even more obscure. It most likely is not associated with any direct effect on the growth process because the epithelial cells in a wounded and cortisone treated animal will continue to proliferate and completely cover the wound even in the absence of significant granulation tissue formation. Attempts to find antagonists for this effect of cortisone have so far been unsuccessful. The inhibition may be related to decreased vas-

cular permeability and possibly to the fact that decreased amounts of fibrin present in the acute inflammatory exudate or in the traumatized area may not form a good scaffold for granulation tissue proliferation.[14] It may also be associated with the fact that the general lymphocytic and mononuclear cell depletion that occurs secondary to cortisone may prevent sufficient precursor cells from which fibroblasts develop from being present at the site of injury. It has also been demonstrated that once granulation tissue is present the use of cortisone will not interfere with the progress of this granulation tissue into compact fibrous tissue and that there will be no lytic effect on the pre-existing granulation and fibrous tissues.[13] This phenomenon of cortisone inhibition of granulation tissue formation is not without its confusing aspects. Cases have been recorded, particularly those of cortisone treated polyarteritis,[15,16] where there seems to have been an unusually rapid fibrosis of the blood vessel lesions. Marked fibrous and healed lesions have been seen to a degree never before recorded in the untreated course of polyarteritis. This has resulted in obliteration of these blood vessels with consequent harmful and fatal effects particularly where the kidney has been involved. Thus on the one hand cortisone is known to inhibit granulation tissue formation and yet in certain instances there seems to be evidence that an unusually rapid fibrosis has taken place in the presence of cortisone. Again it may be a question of the virulence of the stimulating agent as opposed to the dose of cortisone. An important factor may be the stage of the disease in which cortisone has been employed.

Controversy has centered around the effects of cortisone on the antigen-antibody reaction. The original observations that cortisone suppresses tuberculosis sensitivity have not been entirely confirmed.[17-19] Some of the original concepts that ACTH and cortisone profoundly affect the formation of antibody also have not been substantiated.[20-22] Some of the earlier observations that the pituary-adrenal axis mediated through cortisone promote the release of antibody from the lymphocytes remains unconfirmed. There have been studies showing that ACTH has not prevented the histamine effects on the intestinal strip of guinea pigs.[23] ACTH has also not prevented anaphylaxis reactions in vivo and in vitro in active or passively sensitized guinea pigs. It has also not prevented normal titers of antibody to pneumococcal polysaccharides from being formed in humans.[24] Numerous other studies tend to confirm these latter reports. However, there are certain indications that there may be species differences in this respect. It would appear, therefore, that whatever effects have been obtained in altering sensitivity or immune reactions may be entirely non-specific and not intimately related to this antigen-antibody mechanism.

Certain other general effects of cortisone are also of extreme importance in understanding the effects obtained in certain pulmonary conditions. A decrease in the quantity of circulating fibrinogen has been recorded in the human while under the influence of cortisone.[25] This may be a factor in the non-specific drop in sedimentation rate that occurs during the administration of these hormones. There is an increase in the coagulability of the blood in the human during cortisone therapy.[26,27] The sodium and

water retention and catabolic effects of these hormones are too well known to require further discussion. The effects on hyaluronidase are still not clear.[28] These then are some of the basic biological effects of cortisone which must be taken into consideration in the consideration and evaluation of these hormones for the use in any specific pulmonary condition.

Some of the prior mentioned effects of cortisone are illustrated in its use in acute inflammations of the lung. Kass, Ingbar and Finland[29] have investigated the effects of adrenocorticotropic hormone in both pneumococcal and atypical pneumonia. They observed a rapid defervescence with prompt relief of symptoms and disappearance of evidence of toxemia. However, pneumococci were present in large numbers in the sputum for considerable periods of time after the patients had become afebrile and asymptomatic. In one patient bacteremia was present 36 hours after the patient had become clinically well. They found no interference with antibody formation and noted that the pneumococci were not phagocytized in the usual manner. One case developed empyema while under therapy. In one case of atypical pneumonia there was a return of fever and malaise after the ACTH was discontinued. Cold agglutinin formation was not interfered with. Despite the ACTH, one patient developed sensitivity to aureomycin. No specific anti-bacterial action of the ACTH was demonstrated. It can be seen that these agents are not curative in any strict sense since the bacteria persisted in great numbers in the sputa and in one instance bacteremia was present. The beneficial effects were obtained by regulating the severity of the inflammatory process. This raises the key question, of course, of how far it is possible to interfere with this inflammatory process and not get into serious trouble. Unquestionably an extensive inflammatory response to a noxious agent, particularly in the lungs may produce serious consequences. With more experience and with perhaps proper combinations of antibiotics it may prove to be beneficial to regulate this process. Our present knowledge concerning this still remains meager. Also illustrated by the use of ACTH in the above cases was the fact that the antigen-antibody reaction was not significantly interfered with, at least to the extent that pneumococcal and cold agglutinins appeared in the expected titers. The bacteremia again illustrated the fact that the use of ACTH and cortisone interferes with the ability of the body to localize infectious agents.

In a personally observed case of active rheumatic fever with so-called rheumatic pneumonia large doses of ACTH and cortisone failed to significantly alter the extent of the mononuclear exudate in the lungs.[30] In another instance the infection in a bronchiectasis flared up while cortisone was being used for another reason. Cases treated with cortisone for a wide variety of conditions have developed pneumonia with the symptoms masked because of the suppression of the inflammatory exudate and the general feeling of well-being that so often accompanies this form of therapy. Such cases that have been necropsied have revealed a histologic picture of pneumonia that was similar to that seen in agranulocytosis[31] (see Figure 1). The lungs contained relatively few polymorphonuclear leucocytes, scant

fibrin despite the presence of overwhelming numbers of bacteria. This picture was similar to that seen in streptococcal pneumonia in cortisone treated rabbits.[32] In other experimental studies the resistance of mice to pneumonia virus (PVM) was considerably lower.[33] Streptococcal lymphadenitis and pneumonia in mice ran a more fluminant course in those animals receiving cortisone.[34] In these animals there was an interference with the mobilization of the phagocytic cells at the site of infection. In mice it is possible to produce fibrinous pneumonia by subjecting animals to exposures of high oxygen tension. Cortisone markedly lowers the survival rate of animals exposed in this manner.[35] In addition the pneumonic consolidation developed much earlier despite the fact that cell content of the exudate was considerably less than that of the pneumonic consolidation which developed much later in the untreated animal.

It is conceivable that cortisone might prove to be extremely useful in various forms of acute chemical pneumonia such as that following phosgene exposure. In this instance the suppression of acute inflammatory exudate might relieve the anoxia and acute cor pulmonale and prevent the development of bronchiolitis fibrosis obliterans. Even in this acute situation where the original noxious agent is no longer present the possibility of secondary streptococcal invaders must be considered so that again the problem of the immediate control and localization of bacteria is encountered.

It is quite obvious from these clinical and experimental experiences that the effect of cortisone is on the host and not on the bacteria or other inciting agent. Thus ACTH and cortisone have accentuated the problems

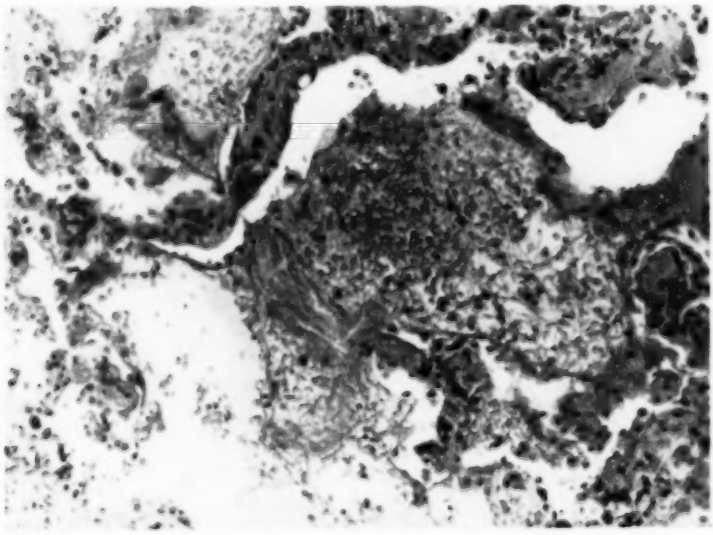

FIGURE 1: Photomicrograph of lung showing pneumonic exudate devoid of polymorphonuclear leucocytes.
(Case shown through courtesy of Dr. L. Sokoloff, Bellevue Hospital).

forcefully brought into prominence by the sulfonamides and by the antibiotics. What exactly is the nature of inflammation? When is an inflammatory reaction useful, and when does it become harmful?

The effect of cortisone on the tuberculous process is now well known. Numerous experimental studies have shown that not only is it harmful to the host's resistance but will also to some extent negate the beneficial effects of concurrent streptomycin therapy.[36-40] Reports on the use of ACTH and cortisone directly for tuberculosis and in non-tuberculous conditions with the subsequent appearance of active tuberculosis give clinical support to the original experimental observations.[41-44] The prior discussed mechanisms such as a depletion in lymphocytic and mononuclear cell reserves; the interference with the inflammatory process and in particular the inhibition of granulation tissue formation are most likely important factors in this phenomenon. Just as the search for a substance to treat arthritis originated with the fact that during pregnancy there was an amelioration of the symptoms and signs of the rheumatoid arthritis so one may reason that the harmful effects of pregnancy on pulmonary tuberculosis might also be related to an increase in cortisone or similar substances. It has been estimated by bio-assay techniques that there is a significant rise in endogenous cortisone production during the eighth month of pregnancy.[45] For many years arguments have raged over the value of prolonged bedrest in the treatment of tuberculosis. Those clinicians who claimed beneficial results from bedrest treatment were never adequately able to explain the reason on a sound physiological basis. Discovery of cortisone and its effect on tuberculosis may provide a strong argument for the use of strict bedrest in the treatment of tuberculosis. It has been demonstrated that endogenous production of cortisone under medical stress conditions may be quite significant.[45] In some instances it has been estimated that in stress situations endogenous cortisone levels have almost approached those seen following therapeutic doses of ACTH. Bedrest with the consequent removal from the stress and strains of everyday life undoubtedly lowers the endogenous cortisone output. This in turn must surely have a beneficial effect on those factors concerned with the host's resistance to tuberculosis. It may be that this mechanism is more important in the bedrest treatment than any of the mechanical circulatory changes in the lung that have been described previously.

It should be emphasized that a minimal precaution that should be taken before ACTH and cortisone therapy is instituted for any reason is a routine chest film to exclude the possibility of any latent or incipient tuberculous focus. However, even with this precaution an unforeseen harmful sequence of events may ensue. The author has observed a case with a previously negative tuberculin test and a clear chest x-ray picture that developed disseminated tuberculosis following the use of cortisone. Another case of reactivation of arrested pulmonary tuberculosis has also been observed.

In regard to the effect on tuberculin sensitivity the work of Reinnuth and Smith is of great interest.[46] Sensitized rabbits respond with extensive acute pneumonic consolidation to intra-tracheal injections of tuberculin

in 100, 125, and 250 mg. doses. In the sensitive animals the reaction reaches a maximum between the second and fourth days and disappears between the sixth and twelfth days in most animals. Sensitive rabbits treated with ACTH showed less pneumonic consolidation. However, if the therapy was discontinued between the fourth and thirteenth day and the rabbit sacrificed, several days later fresh acute areas of pneumonic consolidation similar to that seen in the initial reaction of the control animal. This again illustrates temporary suppressing effect of these hormones. Persistence of the antigen beyond the duration of the therapy then produced an acute reaction. It is important to realize that recent studies indicate that antigens may persist in the body for very long periods of time.

At present we are carrying out studies with cortisone doses much smaller than any previously used to evaluate the effect in association with streptomycin on tuberculous lesions.[47]

The problem can best be summed up by a quotation from an editorial in the British Medical Journal: "Cortisone may eventually prove to have no beneficial influence on tuberculosis, although its possibilities have certainly not yet been explored. Tuberculin in large doses can cause an exacerbation and spread of the disease, but its administration in small increasing doses over long periods has been advocated repeatedly during the last 60 years in certain types of infection. Among therapeutic possibilities it might be suggested that cortisone or tuberculin could be used to flush the bacilli from the lesions while streptomycin and PAS shoot them down. To employ such speculative manoeuvres would require great faith in the discrimination of the beaters and the accuracy of the guns." The applicability of these experimental observations to the human problem relative to certain cortisone effects has been questioned. It has been claimed that dosage levels used experimentally were much too high and not comparable to therapeutic levels used in man. For this reason we repeated the spleen size, wound healing, and acute inflammation experiments in mice using graded doses of cortisone ranging from 0.00025 mg. through 4 mg. daily, and found effects in spleen size, wound healing, and acute inflammation at the 0.025 mg. level. This dose level on a weight basis is comparable to 50 mg. dose in a 70 kilogram man. Therefore, this objection does not appear to be valid.

One of the most promising fields for the use of these formones in pulmonary disease is in the chronic granulomatous inflammation, in particular Boeck's sarcoid and beryllosis.[48-50] Up to the advent of these hormones there was nothing that would have any effect on these conditions. The problem is two-fold; to eliminate the active inflammatory process and to prevent the development of further fibrosis. In acute beryllosis the histologic picture consists of an intra-alveolar edematous exudate, the predominant cell of which is the mononuclear. Death may result from asphyxia with or without acute cor pulmonale. The use of an agent to suppress and eliminate this inflammatory process may be lifesaving. In the chronic form of beryllosis the lesions are predominately interstitial, chronic, and granulomatous. The right side of the heart may be hyper-

trophied and death may be due to chronic pulmonary insufficiency and chronic cor pulmonale. The use of cortisone will often cause the disappearance of the epithelioid or mononuclear cells from the granuloma. This has relieved the strain on pulmonary function and has resulted in temporary increase in maximum breathing capacity and some increase in lung volume. The suppression or elimination of the granulomatous exudate in the alveolar walls will result in an improvement of alveolar-capillary diffusion. The cortisone can not eliminate the fibrosis that is already present nor can it apparently neutralize or aid in the elimination of the beryllium. Even though striking immediate improvement may result, it is probably too much to expect a complete or long term elimination of the disease. Further study is obviously required. Numerous reports on the use of these hormones in beryllosis have been encouraging with resultant symptomatic and functional improvement. Following interruption of therapy regression has been observed in some patients demonstarting the chronic form of the disease.

The same problem exists in Boeck's sarcoid. A peculiar hyalin-like material will then replace the original granulomatous infiltration. This material has not been clearly identified. Kveim reaction after the use of cortisone will not result in the typical granulomatous lesion but will produce a relatively acellular hyalin appearing picture (see Figures 2 and 3). However, in addition to the pulmonary involvement there may be serious eye involvement and although the cortisone may not be curative, it may

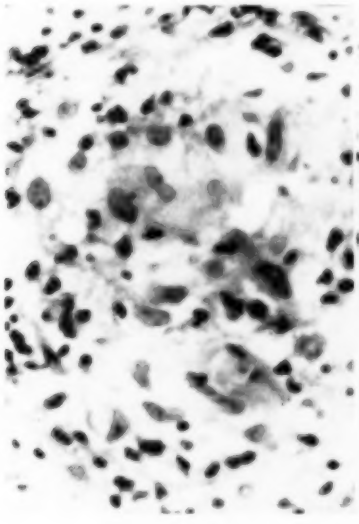

FIGURE 2

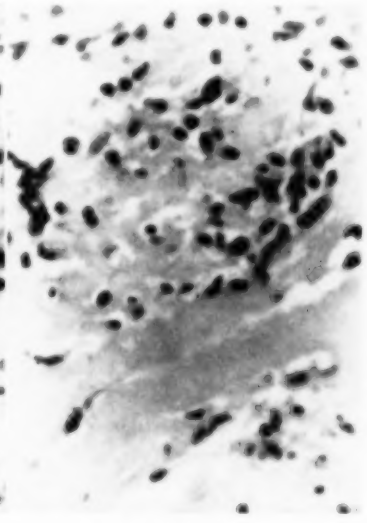

FIGURE 3

Figure 2: Photomicrograph showing typical lesion of Boeck's sarcoid before cortisone therapy. (Case through courtesy of Dr. M. Kushner, Bellevue Hospital). — *Figure 3:* Photomicrograph showing hyaline change in Boeck's sarcoid lesion following cortisone therapy.

prevent scarring in the eye which might result in blindness. The case reported by Siltzbach is striking testimony to the value of the use of cortisone, particularly for the eye changes.[51] Rather prolonged regression of symptoms has been observed even after treatment has been stopped.[52] Clearing of the pulmonary infiltrate has occurred within six days of the onset of treatment. Other reports indicate failure to note any improvement. These cases most likely were in the endstage of granulomatous reaction. Before instituting therapy one must be reasonably sure one is dealing with Boeck's sarcoid and not tuberculosis. The failure of active tuberculosis to develop in those cases of Boeck's sarcoid treated with cortisone and ACTH would tend to support the view that at least some cases of Boeck's sarcoid are of a non-tuberculous etiology. Cortisone has been tried in chronic fibrosis with emphysema. The rational for its use in this situation is not clear since it has been demonstrated that it will not affect pre-existing fibrous tissue. On the contrary its use might be associated in this instance with great danger. Particularly in those cases of emphysema where pulmonary hypertension is present. The salt and water retention induced by cortisone might then precipitate right-sided heart failure. Silicosis presents essentially the same problem. There is very little mononuclear cell infiltration and it would require a lifetime of treatment to attempt to prevent the development and progress of fibrosis. Aside from other considerations the danger of complicating tuberculosis would preclude its use.

The successful use of ACTH and cortisone in intractable bronchial asthma requires little further documentation. The mode of action, however, still remains obscure. That the action is mediated through alteration of the antigen-antibody mechanism is extremely doubtful. Leith et al.[53] reports on the failure of ACTH to significantly alter the positive scratch on passive transfer skin tests in 10 hay fever patients despite disappearance of active symptoms in four cases while under ACTH therapy. Cooke et al.[54] in reporting on the effects of ACTH and cortisone in asthma, dermatitis, and urticaria demonstrated the favorable symptomatic effect but noted that there were little lasting effects while the causative factor continued to operate. Immunological studies conducted by them indicated that symptomatic benefits resulting from hormonal therapy were not due to interference with the immediate wheal type reaction of antigen-antibody sensitized cells. The studies of Feinberg et al.[55] confirm these observations. On the other hand it has been shown that adrenalectomy has enhanced the immunologic reactions of hyper-sensitiveness in rabbits. This included anaphylaxis, precipitin titer, and Arthus phenomenon. Unquestionably the relationship of these hormones to manifestations of bronchial asthma require further study. An interesting phenomenon is the development of sensitivity to cortico-trophin itself.[56] This is a strange occurrence since this material is supposed to relieve the symptoms and signs of hypersensitivity. The relationship of Loeffler's syndrome, allergic granulomatosis of the lungs, and polyarteritis involving the lungs also requires further investigation.

Associated with the use of these hormones is the possibility of an increased incidence in thrombo-embolic episodes and multiple pulmonary emboli. This is based upon the fact that hyper-coagulability of the blood is induced by these hormones.[57]

Whether or not these hormones are the "miracle" drugs or as Cecil has stated merely "glorified forms of aspirin" remains to be seen. At any rate no one can deny the vast possibilities that have been opened for the understanding and study of the pathogenesis of many forms of disease by their discovery.

SUMMARY

Some of the basic effects of cortisone have been described. These include the effects on the inflammatory process, on granulation tissue, and on the antigen-antibody mechanisms. These effects have been related to the clinical results obtained with the use of these hormones in such varied conditions as acute forms of pneumonia, tuberculosis, Boeck's sarcoid, beryllosis, and bronchial asthma.

RESUMEN

Se han descrito algunos de los efectos básicos de la cortisona. Entre ellos se encuentran los efectos sobre el proceso inflamatorio, sobre el tejido de granulación y sobre los mecanismos de antígenos-anticuerpos. Estos efectos han sido relacionados con los resultados clínicos obtenidos con el uso de estas hormonas en tan variados padecimientos como las formas agudas de neumonía, tuberculosis, sarcoide de Boeck, berilosis y asma bronquial.

RESUME

L'auteur décrit quelques effets de base de la cortisone. Il y comprend l'action sur les processus inflammatoires, sur les tissus de granulations, et sur le mécanisme des anticorps et antigènes. Ces faits sont étudiés en relation avec les résultats cliniques qui ont été obtenus après usage de ces hormones dans des affections pulmonaires variées. Il s'agit de formes aigues de pneumonie; de tuberculose, de maladie de Besnier-Boeck-Schaumann, de bérylliose et d'asthme bronchique.

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The Etiology of Pericarditis*

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Approximately 50 years ago Preble[1] analysed the etiologic factors in 244 cases of pericarditis. With the changing age of the population and with more effective methods of treatment, the etiologic factors should be altered, the incidence of certain types of pericarditis lowered, and other types increased.

Source of Material

A survey of 23,288 consecutive autopsies performed in the Los Angeles County Hospital during the 12 years of 1937 through 1948 was carefully reviewed with reference to the disease process causing the pericarditis.

Analysis of Data

There were 1389 cases of pericarditis found. This is a total incidence of 6.0 per cent. Table I which follows shows the etiologic factors and the incidence of each factor.

Comment

The autopsy incidence of pericarditis is not identical with the clinical incidence. Some patients who have clinical pericarditis recover leaving no pathological sign of the lesion; while a larger number of patients have pericarditis which escapes clinical recognition and is found only at autopsy. In 1945 the author[2] reported a clinical incidence as 2.82 per cent pericarditis in active rheumatic fever patients. One hundred per cent of the patients with active rheumatic fever studied at autopsy showed gross and histologic evidence of rheumatic pericarditis. Minimal pericarditis may not be recognized clinically by our present methods of study. Conversely, a clinically recognized pericarditis may recover, leaving no sign at autopsy by which the etiology can be determined.

The high incidence of idiopathic pericarditis is illustrative. Chronic fibrinous pericarditis, such as local milk patches or adhesive obliterative pericarditis, may give no clue as to the etiology. When the high incidence of rheumatic pericarditis, 13.8 per cent, is added to the 15.8 per cent incidence of idiopathic pericarditis, the total closely parallels Preble's 28.4 per cent incidence of rheumatic pericarditis.

The high incidence of septicemic pericarditis, 10.4 per cent, must be viewed with the knowledge that in most of the cases the septicemia was of such severe degree as to cause death. It is not known whether the nonfatal septicemias have any direct or proportional effect on the incidence of pericarditis. Since the antibiotics have come into general use there is a decrease in septicemic pericarditis.

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TABLE I: ETIOLOGY OF PERICARDITIS

	1937	*1938*	*1939*	*1940*	*1941*	*1942*	*1943*	*1944*	*1945*	*1946*	*1947*	*1948*	*Total*	*Pct.*	*Preble Pct.-1901*
Idiopathic	17	26	7	20	16	15	15	13	17	17	31	26	220	15.8	
Rheumatic	17	22	24	18	19	16	12	14	8	13	11	17	191	13.8	28.4
Septicemia	18	12	14	14	18	12	18	15	10	11	2	4	148	10.7	4.7
Tuberculous	7	15	13	15	9	3	2	4	4	4	10	10	96	6.9	10.0
Lobar Pneumonia	3	4	4	4	2	3	1	2	2	1	1	2	29	2.1	34.5
Bronchopneumonia	3	6	5	3	2	2	3	2	1	2	1	2	32	2.3	
Chronic Lung Pathology	3	9	7	6	4	2	1	1	1		5		39	2.8	
Uremic	12	10	16	17	14	17	21	21	13	12	31	22	206	14.8	11.0
Acute Myocardial Infarction	11	25	15	15	13	11	10	6	9	13	7	9	144	10.4	2.6
Chronic Coronary Artery Disease	25	26	6	11	10	16	9	2	4	8	12	8	137	9.9	
Metastatic Carcinoma	10	13	12	7	9	2	12	8	7	9	5	16	110	7.9	
Metastatic Sarcoma			1		4	2	1	2	2		1	1	14	1.0	
Disseminated Lupus Erythematosis		1			1		1		1		1	2	7	.5	
Acute Leukemia			2		1	1							4	.29	
Coccidioidomycosis		2			1							1	4	.29	
Lymphoblastoma Actinomycosis	1				1						1		3	.22	
Rheumatoid Arthritis		2										1	3	.22	
Total Each Year	127	173	127	130	124	102	106	90	79	90	119	122	1389		
Autopsies Each Year	2070	1966	2171	2308	2185	2109	1801	1638	1537	1785	1895	1833	23,288		
Percentage Each Year	6.1	8.3	5.8	5.6	5.6	5.1	5.9	5.5	5.1	5.0	6.3	6.7	6.0		

The decrease in the incidence of tuberculous pericarditis is commensurate with the decreased mortality rate from this disease and is especially low in this series of autopsied cases, because during the war years cases of tuberculosis were cared for in private institutions. Following the war more cases again came to autopsy in the general hospital.

The very marked fall in the incidence of pericarditis occurring from fatal pneumonias is believed to be due to the successful use of the chemotherapeutic and antibiotic drugs.

The high incidence rate of uremic pericarditis and of pericarditis secondary to cardiovascular diseases and malignancy is due to the change in the age distribution of the population.

The rise in the incidence of pericarditis associated with the diseases of older age groups causes the total incidence to be moderately higher than that reported by Preble[1] (4.1 per cent) in 1901 and that reported by Smith and Willius[2] (4.2 per cent) in 1932.

We wish to acknowledge with thanks the cooperation of Professor Edward M. Butt for making available the material for this study.

SUMMARY

1) The general autopsy incidence of pericarditis is 5.95 per cent. This figure changes very little from year to year.

2) The incidence of pericarditis due to bacterial invasion is definitely decreased since the advent of the chemotherapeutic and antibiotic agents.

3) Pericarditis secondary to uremia, cardiovascular diseases and malignancy are increased as the population grows older.

RESUMEN

1) La frecuencia general de la pericarditis en la autopsia es de 5.95 por ciento. Este número cambia muy poco de año en año.

2) La frecuencia de la pericarditis debida a la invasión bacteriana ha sido definitivamente disminuida desde el advenimiento de los agentes quimioterápicos y antibióticos.

3) La pericarditis secundaria debida a la uremia, las enfermedades cardiovasculares y malignas aumentan con la ancianidad de la población.

RESUME

1) D'après les constatations d'autopsie, l'incidence générale de la péricardite est de 5.95%. Le taux change peu d'année en année.

2) La fréquence de la péricardite infectieuse est nettement en régression depuis l'apparition des agents chimiothérapiques et antibiotiques.

3) Par contre, il y a une augmentation des péricardites secondaires à l'urémie, aux affections cardiovasculaires, et aux tumeurs malignes en fonction du vieillisement de la population.

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Pericardial Celomic Cyst*

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Pericardial cysts have been described from time to time in medical literature. They would appear to be more common than one would infer from the number of clinical reports. Most of the articles deal with post mortem study or surgical experience, since the diagnosis is rather difficult to make ante mortem. However, pericardial cysts may usually be suspected ante mortem because of the changes visible on x-ray examination of the chest. These cysts are large, round masses characteristically found in the anterior, inferior portion of the mediastinum, chiefly on the right side. They usually bulge toward the pleural space. The nature of these cysts is such that they are represented roentgenologically by a round homogeneous density with smooth contour and sharply demarcated border. Ordinarily, the density differs from that of the heart, does not pulsate, and does not expand with cardiac systole or with respiration. It is true that because of compression, these cysts sometimes produce symptoms such as cough, dyspnea and pain, but there is no clinical syndrome sufficiently characteristic to permit diagnosis on the basis of the history. Physical examination and laboratory tests other than radiographic are of no assistance.

It is commonly stated that pericardial cysts should be removed because they sometimes become malignant. Their greatest significance is probably in the differential diagnosis of other chest lesions, such as, epicardial fat pad, lipoma or other benign tumors, dermoid cysts, ventricular aneurism, hiatus hernia, pericarditis, pulmonary malignancy and eventration of colon.

Case Report

A.V., a 52 year old white male, was admitted to the hospital on October 22, 1941. The admission diagnosis was schizophrenia, catatonic type. There was no previous history of serious illness other than psychosis which necessitated hospitalization. The admission physical examination was entirely normal except for the blood pressure recording of 154/96. While in the hospital he made a satisfactory adjustment. In February 1947 he appeared moderately dyspneic. At that time physical examination was normal except for the blood pressure reading which ranged from 140/72 to 178/100. On February 12, 1947 he was digitalized with digitoxin and placed on a maintenance dose of digitoxin 0.2 mg. daily. The mild dyspnea soon disappeared. He was inaccessable most of the time and remained rather quiet in the ward. On the evening of July 26, 1948 he retired to bed as usual. The following morning he was discovered dead in bed.

Laboratory data: Chest x-ray examinations on October 24, 1941, October 14, 1946, February 12, 1947 and November 24, 1947 were all normal. Urinalysis on October 23,

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1941 and February 12, 1947 were normal. Electrocardiograms on January 28, 1947, February 17, 1947 and November 14, 1947 were normal except for minor changes transient in nature such as diphasic P II, III. Complete blood count on October 22, 1941 was normal. Serologic test for syphilis on December 3, 1946 was normal.

On post mortem examination, the heart weighed 420 grams. Fifty cc. of clear straw colored fluid was found in the pericardial sac. Attached to the right inferior angle of the epicardial surface by means of a narrow fibrous stalk was a cystic structure lobular in outline and roughly ovoid in shape. The distal extremity was attached to the diaphragmatic pleura on the right side. The cyst measured 6 x 3 x 2.5 cm. The wall of the cyst was thin and transparent. The cyst was filled with clear, pale yellow fluid. The lining was smooth and regular. No communication was found between the cyst and the pericardial cavity. Both parietal and visceral layers of the pericardium were smooth and glistening, except for one area over the anterior surface of the right ventricle which was white and opaque.

The right auricle and ventricle had no significant change. Tricuspid and pulmonary valves were normal. The left auricle and mitral valve were not remarkable. The wall of the left ventricle was thickened and showed several grey streaks. Yellow plaques were seen on the aortic valve cusps and in the sinuses of Valsalva. The coronary arteries had numerous plaques which narrowed the lumen. A firm, hard mass completely occluded the lumen of the left anterior descending coronary artery about 2 cm. from its origin. In the right coronary artery 3 cm. from its origin there was almost complete occlusion of the lumen, only a pin point opening being present.

Microscopic examination of the cyst wall revealed varying thickness of collagenous tissue; in some places this assumed a nodular character with tendency to concentric arrangement. The tissue was relatively acellular. In the deeper layer adjacent to the adventitial loose areolar and fat tissues were several fairly dense collections of round cells. These appeared in the region of dilated capillaries. The lining of the cyst consisted of a single layer of flat cells.

The most commonly accepted explanation of the etiology of these cysts is that put forward by Lambert. He described the origin of the pericardium from a series of disconnected lacunae in the embryonic mesenchyme which antedates the actual formation of the heart. These lacunae are formed lateral and ventral to the primitive streak but later fuse to form a horse-shoe shaped coelomic cavity around the cardiac situs. At first this is an independent cavity but later it communicates with the pleuroperitoneal coelom. Subsequently, the ligamentum transversum and ducts of Cuvier close this communication. Inequality in the rate of development of one of the lacunae which go to form the pericardial coelom results in the formation of a congenital diverticulum of the pericardium. Failure of one of the primitive lacunae to merge with others and its persistence, undoubtedly account for the pericardial cyst which more accurately should be called pericardial coelomic cyst.

SUMMARY

We have presented above the case history and the post mortem and anatomical findings in a case of a 52 year old white male. In this instance the pericardial cyst was not suspected clinically because of complete absence of symptoms. On post mortem review of chest x-ray films there was no evidence of the presence of such a cyst. We feel the unusual feature of this case is the presence of a cyst as large as this one without the production of sufficient changes on chest x-ray examination, to permit diagnosis. Undoubtedly, this may be attributed to similar densities of lung and cyst and to the presence of overlying pulmonary tissue which produced apparently normal lung markings in the area occupied by the cyst.

RESUMEN

Se ha presentado el caso de un hombre blanco de 52 años con los hallazgos de la historia clínica, el post-mortem y los hallazgos anatómicos. En este caso el quiste precardiaco no fué sospechado clinicamente por la ausencia completa de síntomas. La revisión post-mortem de la películas de rayos X no demostró evidencia de quiste. Creemos que la caracteristica más inusitada en este caso es la presencia de un quiste tan grande como este sin la producción de cambios suficientes a los rayos X para permitir el diagnóstico. Sin duda esto puede ser atribuído a las densidades similares del pulmón y del quiste y a la presencia de tejido pulmonar suprayacente que produjo trazos aparentes de pulmón normal en el área ocupada por el quiste.

RESUME

Les auteurs présentent l'observation et les constatations anatomiques post mortem d'un cas de kyste péricardique chez un homme de 52 ans. Dans ce cas, le kyste péricardique n'était pas suspecté cliniquement car il ne s'accompagnait d'aucun symptôme. En revoyant le film radiologique du thorax après la mort il n'y avait aucun signe de la présence de ce kyste. Les auteurs exposent combien est inhabituelle l'existence d'un kyste aussi volumineux, sans qu'il s'accompagne d'aucune modification radiologique qui permette le diagnostic. Il leur parait incontestable que ceci doit être attribué au fait que la densité du poumon et du kyste était semblable, et que d'autre part une zone de tissu pulmonaire s'interposait devant le kyste, lui donnant l'aspect d'une zone pulmonaire normale.

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Primary Carcinoma of the Lung in the Aged*

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Primary carcinoma of the lung occurs most frequently between the ages of 40 and 70 years. It rarely is seen in childhood, but it is not infrequent in the aged. In a series of 849 patients with primary carcinoma of the lung admitted to the Mount Sinai Hospital from January 1, 1935, to December 31, 1947, the age incidence was as follows:

20-29 years	2
30-39 years	21
40-49 years	160
50-59 years	345
60-69 years	277
70-79 years	43
Over 80 years	1

Since the advent of the antibiotics and the other new adjuvants to surgery, there has been an appreciable decrease in the mortality following thoracic surgical procedures. This lowered postoperative mortality has enabled surgeons to extend the indications for surgery into the older age groups, as well as to an increasing number of disease entities, which formerly were surgically "untouchable."

There are not a few physicians who hesitate to subject patients over the age of 65 years to major surgery, even for malignant disease. In the last decade, there has been a significant reduction in mortality following major surgical procedures, and this has been manifest in the older patient as well as in the younger and more favorable surgical risk.

In order to evaluate the results of surgical treatment of primary carcinoma of the lung in the aged, the records of all patients with this disease, 65 years of age or over, seen at the Mount Sinai Hospital from January 1, 1945, to June 30, 1950, have been analyzed. The patients in this age group who were observed in the Tumour Clinic but not admitted to the In-patient Services have also been included. A majority of the latter were considered to be inoperable by the Clinic staff.

The case histories of 201 patients comprise the material for this report. The age occurrence (Table I) was as follows:

65-69 years	62
70-74 years	34
75-79 years	3
Over 80 years	2

Eighty-five were males and 16 were females.

Frequently, in the recorded histories, a number of symptoms were listed as the initial ones: therefore, it was not always possible to decide which

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one actually was the first to occur. However, this has been determined as accurately as possible from the charts. The occurrence of the first symptoms is listed in Table II. It is apparent that the onset of the disease was characterized by either cough and sputum or pain in almost two-thirds of the patients. The tumour was discovered during a routine check-up of the two patients listed under the asymptomatic heading.

The duration of symptoms of carcinoma of the lung in relation to operability has been a subject which has received considerable attention. In a plea for earlier diagnosis and surgical exploration, much has been written concerning the interval of time which elapses between the onset of symptoms and operation. Comparisons have been made between the delay of the patient in seeing a physician and the delay of the physician in making the diagnosis and referring the patient for surgery.

Table III shows the relation between the duration of symptoms and operability. In 14 patients who were seen within one month of the onset of symptoms, the tumour was not resectable. Of 66 patients with symptoms less than six months in duration, including the previously mentioned 14, resection was possible in only 12 (18 per cent). In 33 who had had symptoms for more than six months, resection was possible in seven (21 per cent); and one patient who had had symptoms for three years had a resectable carcinoma.

In every case, an attempt was made to make a pathologic diagnosis of carcinoma, even in those patients who were considered inoperable on clinical grounds. Bronchoscopic examination was performed on 58 patients, and specimens removed for biopsy were positive for carcinoma in 38. Lung aspiration yielded malignant tissue in seven, and malignant cells were found in the pleural effusions of five. Nodes removed for biopsy were positive in five, and specimens aspirated from metastatic foci were positive in four. Papanicolaou smears of bronchial washings were positive in five cases; in these, specimens removed for biopsy were also positive.

Sixty-seven per cent of the patients were found to be inoperable when first examined; this coincides with the rate of inoperability in series comprising all age groups as seen in general hospitals. Table IV lists the reasons for not subjecting these patients to operation. In those over the age of 65, one would expect that a considerable number would be refused operation because of age, poor general condition, lowered respiratory function, or the presence of a serious constitutional disease which would contraindicate the performance of any major operation; yet only eight patients fell into this category. Two were dyspnoeic and cyanotic at rest; one had marked weakness and generalized senile tremors; another had

TABLE I: Age and Sex

	65-69 Years	70-74 Years	75-79 Years	Over 80 Years
Male	50	31	3	1
Female	12	3	0	1
TOTAL	62	34	3	2

TABLE III: Duration of Symptoms and Operability.

DURATION	NOT OPERATED	OPERATED	
		Exploration Only	Resected
Less than one month	11	3	
One to three months	19	1	7
Three to six months	16	4	5
Six to twelve months	8	3	4
One year	4		2
Two years	7	2	
Three years	1		1
Eight years	1		
No symptoms	1		1
TOTAL	68	13	20

TABLE II

First Symptoms

Cough and sputum	*38
Pain	26
Weakness and loss of weight	7
Hemoptysis	7
Dyspnoea	5
Pneumonia	5
Metastases (bone—skin)	5
Hoarseness	3
Asymptomatic	2
Cerebral metastases	2
Pulmonary osteoarthropathy	1
TOTAL	101

*Thirty-three patients had bloody sputum without frank hemoptysis.

TABLE IV

Reasons for Clinical Inoperability

Osseous metastases	18
Died shortly after admission	8
Age—dyspnoea—general condition	8
Malignant cells in pleural fluid or massive bloody effusions	7
Extrathoracic metastatic nodes	6

TABLE IV (Continued)

Cerebral metastases	4
Tumour invading the carina	4
Contralateral pulmonary metastases	3
Refused operation	3
Massive mediastinal nodes	2
Nerve involvement	2
Superior vena cava obstruction	1
Skin metastases	1
Pulmonary tuberculosis	1
TOTAL	68

TABLE V

Types of Cells

Squamous cell	33
Immature or anaplastic squamous cell	14
Adenocarcinoma	8
Anaplastic adenocarcinoma	1
Mucous cell adenocarcinoma	1
Columnar cell carcinoma	1
Squamous cell plus mucinous adenocarcinoma	1
Small cell	4
TOTAL	63

an aneurysm of the descending aorta; the fifth had electrocardiographic changes compatible with an old myocardial infarct, and a vital capacity of 1.2 liters, 33 per cent of normal; in two, the general condition was such as to indicate an inability to withstand surgery; and the eighth patient had been in cardiac failure on numerous occasions.

A pathologic diagnosis of carcinoma was made in 76 of the 101 cases. Although the diagnosis of carcinoma was made in 13, it was not possible to determine the type of cell. The classification of the remaining 63 is listed in Table V. Of the 20 tumours which were resected, 12 were squamous cell carcinoma; four, immature squamous; two, adenocarcinoma; one, anaplastic adenocarcinoma; and one, squamous cell plus mucinous adenocarcinoma.

Thirty-three patients in this series were operated upon. In 13, the findings at operation precluded the possibility of resection. Most often, the cause was direct extension of the tumour into the mediastinum. There were two postoperative deaths in these exploratory thoracotomies. One occurred on the second day as a result of cardiac failure; the other on the ninth postoperative day. The latter was in a 73 year old man who was found to have a huge necrotic tumour mass widely invading the thoracic wall. The wound was left open and roentgenotherapy was administered.

Twenty patients, all males, were subjected to pulmonary resection. Their ages were as follows:

65 years	4
66 years	2
67 years	1
68 years	3
69 years	2
70 years	4
71 years	1
73 years	2
76 years	1

The duration of symptoms ranged from two months to three years. Three patients had electrocardiographic changes preoperatively, indicating myocardial abnormalities.

Anesthesia was administered endotracheally, using various combinations of nitrous oxide, ether, ethylene, and cyclopropane. The duration of operation was usually from two and one-half to three hours.

The postoperative course of these elderly patients is of great interest. There were two postoperative deaths. One patient died on the operating table from cardiac arrest. Another died on the first postoperative day as a result of a cerebral accident—an operative mortality of 10 per cent. The postoperative hospital stay of the 18 survivors ranged from 11 to 52 days, with an average stay of 22 days. Eight were discharged within two weeks after operation.

Eight patients had an entirely uneventful convalescence. Five developed cardiac arrythmias. Four of these responded within a few days to either digitalis or quinidine, or both; one required 14 days for the return of normal rhythm. Three required bronchoscopic aspirations because of inability to expectorate. Two developed empyema, requiring drainage. One developed severe dyspnoea and dysphagia, the reason for which could not be determined. He required a second admission, during which the symptoms disappeared; he has remained well to date.

The follow-up period for some of the cases in this series has been so

short that only a report of interval results is warranted. In patients in this age group, death may be due to causes other than a recurrence of the original disease. Therefore, it is difficult at times to evaluate the result of the operative procedure upon the malignant process.

Of the 18 patients who survived operation, 10 either developed metastases or died from carcinoma from three to 28 months after operation. Three who were discharged died approximately two months after operation. One death was probably due to cardiac failure; the second, from a cerebral accident which may have been secondary to a metastasis; and, in the third, the cause was unknown.

Five patients are considered to have had interval good results from operation. Two are alive and well. Of the three who died, one had gained 25 pounds and was in good health when, two years after operation, he suddenly expired while sitting in the park. Postmortem examinations were obtained in the other two. One had developed a lobar pneumonia in his remaining lung 11 months after operation. Necropsy revealed lobar pneumonia, rheumatic heart disease, and pulmonary oedema; there was no evidence of recurrent carcinoma. The other died 31 months after pneumonectomy. Postmortem examination revealed an organizing pneumonia in the remaining lung, and there was no evidence of carcinoma.

Of the two patients who are alive and well, one is the oldest in this series. He had a pneumonectomy three and one-half years ago. His only complaint is of dyspnoea upon exertion. He is now 79 years old. The second was 68 years old, in March 1950, when he had a pneumonectomy for a squamous cell carcinoma. He was readmitted in December 1951, with intestinal obstruction due to an adenocarcinoma of the colon. A colonic resection was performed and he is well, 30 months post pneumonectomy.

Discussion

Primary carcinoma of the lung, unless surgically excised, is a fatal disease. It may progress slowly in a small number of patients, but in the great majority, it causes death within one to two years. It is therefore imperative, whenever possible, to attempt to cure this disease by surgical excision. The age of the patient alone should be no contraindication to surgical intervention. The patient's chronologic age is frequently not comparable to his physiologic age. Therefore, they should be studied from the physiologic standpoint. The physician also should appreciate that there are few constitutional diseases which contraindicate surgery for cancer. The status of present day thoracic surgery is such that advanced age should no longer be a deterrent to an attempt at surgical cure of pulmonary carcinoma.

SUMMARY

An analysis of 101 patients with primary carcinoma of the lung is reported. All had passed their 65th birthday. In the main, this series differs very little from larger series of cases which encompass all age groups.

Thirty-three patients were operated upon: 13 were found to be inoperable, pneumonectomy was performed in 16 and lobectomy in four.

A 10 per cent operative mortality in the patients who had resection was conspicuously low, considering their ages. In fact, it compares most favorably with the operative mortality in other large series comprising all age groups.

Postoperative complications responded readily to therapy. Cardiac arrythmia was the most common, occurring in 25 per cent.

The interval result of resection for primary carcinoma of the lung in five patients is considered favorable. Their ages at the time of operation were 66, 67, 68, 70, and 76 years, respectively.

RESUMEN

Se efectúo el analisis de 101 enfermos con carcinoma primario del pulmón. Todos habían pasado los 65 años de edad. En lo fundamental esta serie difiere muy poco de las series más largas de casos que abarcan todas las edades.

Treinta y tres pacientes fueron operados: trece resultaron inoperables y se efectuó la neumonectomía en 16 y lobectomía en cuatro.

La mortalidad operatoria en los pacientes que tenían resección fué de 10 por ciento, notoriamente bajo dadas sus edades. De hecho se puede comparar muy favorablemente estos resultados con la mortalidad operatoria en otras series más largas abarcando todas las edades.

Las complicaciones postoperatorias respondieron prontamente a la terapéutica. La arritmia cardiaca fué la más común, ocurriendo en un 25 por ciento.

El resultado medio de la resección de carcinoma primario del pulmón en seis pacientes es considerado favorable. Sus edades al efectuarse la operación eran 66, 67, 68, 70, y 76 años respectivamente.

RESUME

L'auteur rapporte l'étude de 101 malades, atteints de cancer primitif du poumon. Tous avaient dépassé 65 ans. D'une façon générale, ces cas sont fort peu différents des études plus importantes concernant tous les âges.

33 malades furent opérées: 13 d'entre eux furent considérés comme inopérables; pour 16 autres, on pratiqua une pneumonectomie, chez quatre d'entre eux une lobectomie.

La mortalité opératoire chez les malades qui subirent une résection pulmonaire s'éleva à 10%. Ce chiffre est remarquablement bas, en fonction de leurs âges. En fait, ces cas donnent une statistique plus favorable que celles qui concernent des séries plus importantes de malades, comprenant tous les âges.

Les complications post-opératoires furent facilement jugulées par le traitement. L'arythmie cardiaque fut la plus fréquente, et survint dans 25% des cas.

Le résultat éloigné de la résection du poumon pour cancer primitif peut-être considéré jusqu'à présent comme favorable chez cinq malades. Leurs âges au moment de l'opération était respectivement de 66, 67, 68, 70 et 76 ans.

Hemangio-Endothelioma Arising in a Mediastinal Teratoma*

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This report deals with a case of teratoma of the mediastinum which gave rise to a hemangio-endothelioma with widespread metastases. The case is presented because of its exceeding rarity, and the interesting problems encountered clinically.

Teratomas of the mediastinum have been of sufficient interest to have stimulated a sizeable number of reports in the literature. A considerable amount of information has been recorded as to the developmental aspects, diagnosis, and treatment of this tumor since it was first reported by Gordon[1] in 1827. By 1933, 106 years later, Hedblom[2] collected 185 verified cases from the literature and added six cases of his own. Malignant transformation was present in 17 of the total number. Houghton,[3] in 1936, reported a case of malignant teratoma of the mediastinum, and noted that there were 215 cases in the literature. He then briefly described the 24 accepted and 10 unverified cases of malignant mediastinal teratoma. An extensive review of the subject was published by Rusby[4] in 1944. He tabulated 245 cases of this tumor from the literature up to 1939, and added six of his own. The incidence of cancer in this series was 12.9 per cent. No mention of hemangio-endothelioma arising within a mediastinal teratoma is made by the authors noted above,[1-4] or in the reports,[5-13] published since 1939. Schlumberger[14] presented a documentation of 16 cases of teratoma of the anterior mediastinum. In six of them, the tumor was malignant, presenting itself as an adenocarcinoma in each instance. Willis[15] does suggest the possibility of a vascular tumor arising from a teratoma, but cites no specific case. Thus, the malignant cases reviewed in some detail by Houghton[3] up to 1936 and the available literature published since then, have failed to reveal a case similar to the one being presented.

Inasmuch as there is lack of unanimity concerning the nature and nomenclature of tumors of blood vessels, it is pertinent at this point to define the use of the term hemangio-endothelioma. This is a malignant tumor of blood vascular origin which forms vascular channels of many varieties and is accompanied by proliferation of endothelial cells. The malignant quality of these tumors is based on the cytology and infiltrative growth of the endothelial cells and the incidence of metastases and local recurrence. While the use of the term "angiosarcoma" is nosologically

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desirable (Allen[16]), Stout[17] has preferred to retain hemangio-endothelioma because it is descriptive and frequently used. Stout,[17] in 1943, defined the histologic characteristics of this tumor, considered its relation to other tumors of blood vessels, reviewed the literature and presented a detailed analysis of 18 cases. None of these arose in a teratoma.

Seybold et al.[18] (1948), reported three cases of tumors of blood vascular origin in a group of 200 cases of mediastinal tumor treated surgically. Two of these were hemangioendotheliomas showing histologic evidence of malignancy as well as distant metastases. In a review of the literature on mediastinal tumors, they found 14 acceptable cases of blood vascular tumors of which eight showed evidence of malignancy. None of these were reported to have arisen in or to have been associated with a teratoma.

Case Report

On admission to the Bronx Veterans Administration Hospital, a 33 year old white male automobile mechanic complained of cough, hemoptysis and chest pain of nine weeks duration. He was symptom-free until two and one half months prior to admission when he noted a dull retro-sternal ache which was continuous and aggravated by deep respiration and cough. Several days after the onset, he had a mild cough and expectorated a small amount of thick blood-streaked sputum. He was then admitted to another hospital where x-ray films of the chest revealed a large left upper lobe infiltrate. He was treated with penicillin, aureomycin and streptomycin. Numerous sputa studies for acid fast bacilli were negative. One examination was positive for Friedlander's bacilli. There was no change in the cough or sputum and he was then transferred to this hospital. He denied fever, chills, or night sweats or history of previous pulmonary disease. There was a seven pound weight loss since the onset of his illness.

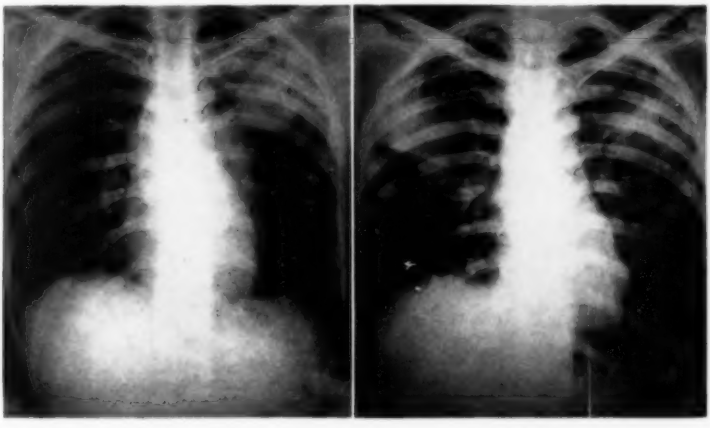


FIGURE 1 FIGURE 2

Figure 1: There is a homogeneous density in the first and second anterior interspaces of the left upper lobe; widening of the superior mediastinum and a rounded density in the right second anterior interspace. — *Figure 2:* X-ray film of chest taken three months after that seen in Figure 1. An extension of the right upper lobe density superiorly and medially, elevation of the horizontal fissure and a decrease in the size of the left upper lobe density are to be noted.

Physical Examination revealed a well developed, chronically ill male not in acute distress. Blood pressure was 122/70. The pulse was 80 and respirations were 20 per minute. The positive physical findings on admission were limited to the chest. There was a small area of bronchial breathing posteriorly in the paravertebral region at the left fourth rib. Slight dullness and diminished breath sounds were found at the left apex anteriorly. There were no rales, cyanosis or significant lymphadenopathy.

Laboratory Data: On admission, the erythrocyte count was 3.4 million, the hemoglobin content was 10.5 grams. The sedimentation rate was 26 mm. per hour. White blood count was 9,600 with normal differential. Repeated smears of sputum concentrates and gastric cultures were negative for acid fast bacilli. The urinalysis was negative. The only positive spinal fluid finding was 150 erythrocytes per cu. mm. X-ray films of the chest (Figure 1) revealed a homogeneous density in the left first and second anterior interspaces localized in the posterior portion of the left upper lobe. There was also noted widening of the superior mediastinum. A rounded density in the right second anterior interspace was observed and this was

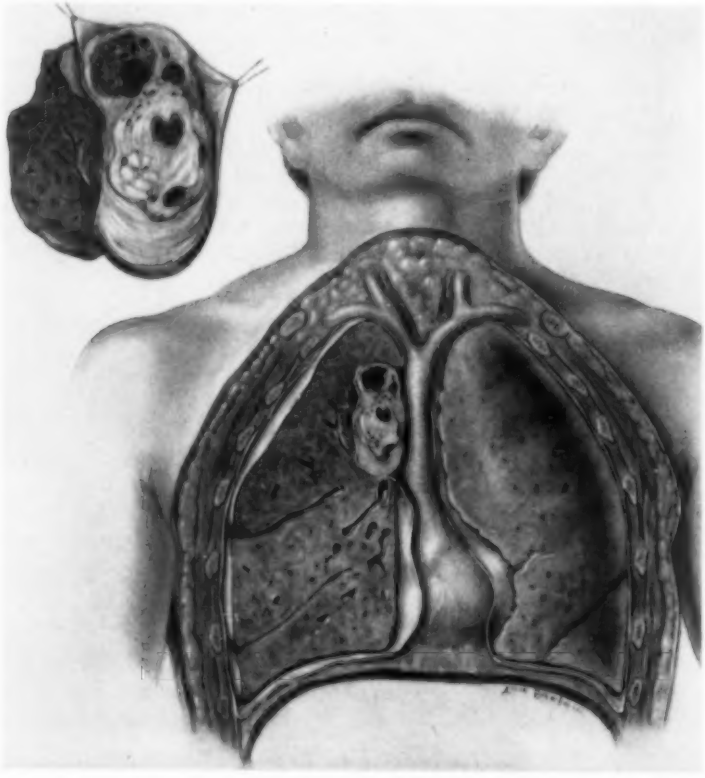


FIGURE 3: Schematic representation of the teratoma in situ. The tumor, although arising in the superior mediastinum, lies in an enclave in the right upper lobe. The insert illustrates the parietal mediastinal pleura which covers the tumor and separates it from the visceral pleura of the lung (for purposes of simplification, the metastatic nodules within the lungs are not represented).

not present in the films obtained from the other hospital. After much discussion the bone survey was considered non-contributory.

The first strength tuberculin test was positive and the coccidioidin and histoplasmin skin tests were negative. Liver function tests, stool examinations, prothrombin time, bleeding, coagulation and clot retraction time were all within normal limits. The ECG revealed sinus tachycardia but no other abnormalitie was noted.

Shortly after admission, he began to complain of severe intermittent pain in the back of his head involving mainly the right side of the neck, the occiput, and extending down to the right shoulder. There was no localizing neurological sign other than hypesthesia and hypalgesia of the right posterior C-3 region. During the first month of hospitalization, he remained afebrile, his cough persisted and there was continued expectoration of several ounces of bloody sputum daily. He was placed on streptomycin 1 gm. and para-aminosalicylic acid 12 gms. daily. At this time, there were noted occasional fine, moist, inspiratory rales over the left anterior superior chest with coarse breath sounds and dullness over the left apex. Para-aminosalicylic acid and streptomycin therapy was discontinued after one month's trial. Repeated blood transfusions were necessary to combat the anemia.

During the second month of hospitalization, the patient's temperature rose daily

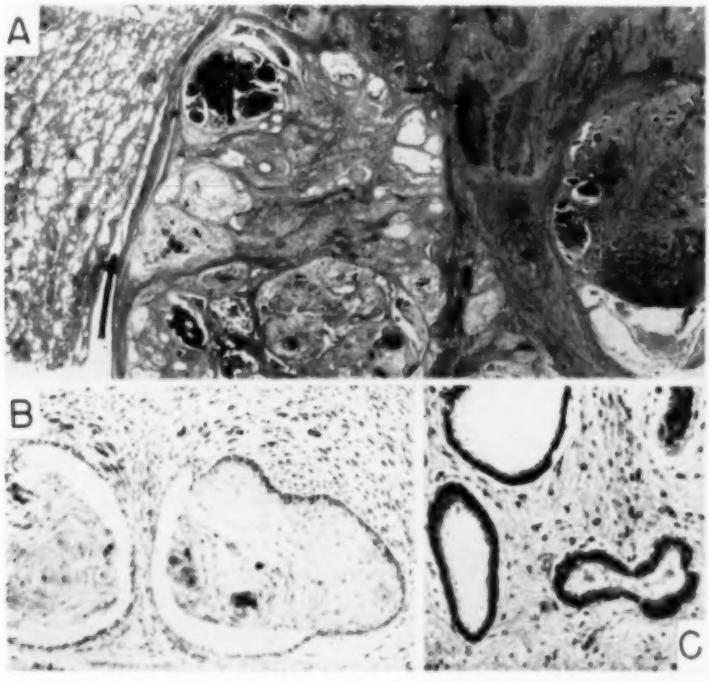
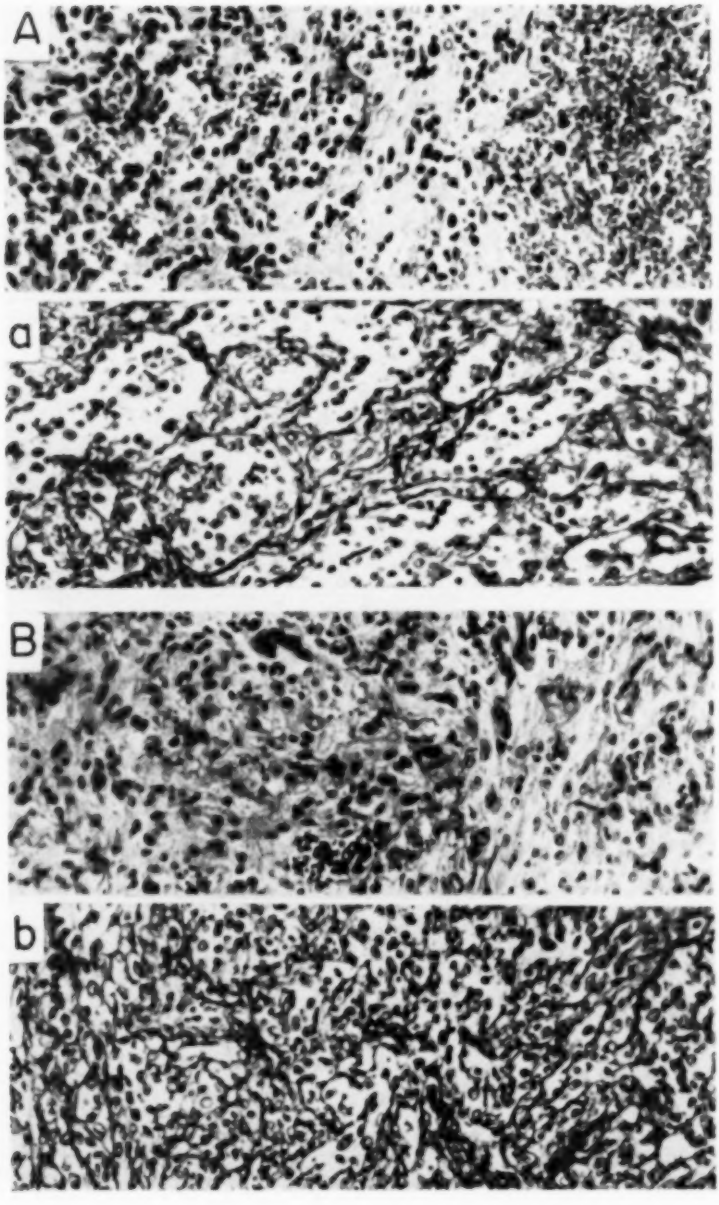


Figure 4A: Low power view of the teratoma and contiguous lung. Arrow points to plane of clearage between tumor and visceral pleura of lung. The tumor is covered by parietal mediastinal pleura. Numerous cystic spaces and hemorrhagic areas within the tumor. (H&E x 7).—*Figure 4B:* Teratoma. Two cavities partly lined by stratified squamous epithelium. Above the cavities, there is a small focus of non-striated muscle. (H&E x 100).—*Figure 4C:* Teratoma. Glandular spaces lined by cuboidal and low columnar epithelium. (H&E x 100).


A
a
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to 100 degrees F. and occasionally to 102 degrees F. Repeat x-ray films of the chest revealed the previously noted widening of the superior mediastinum, an extension of the right upper lobe density superiorly and medially, elevation of the horizontal fissure and decrease in the left upper lobe density (Figure 2). At this time, radiotherapy was instituted over the lesions noted in the chest x-ray films and anterior cervical area. There was little response following four weeks of therapy while 2,500 roentgens in air were delivered to the various lesions. A nasal quality of the voice was noted. Digital examination of the oropharynx revealed a right retropharyngeal mass which was submucosal and extended upward behind the right nasopharynx. Aspirate of this lesion failed to reveal tumor cells and showed only blood clot. Bone marrow examination was non-contributory. His terminal course was one of progressive debilitation, continued hemoptysis and dysphagia. He died after 102 days of hospitalization and six months after the onset of symptoms.

Necropsy

Gross Examination: The body was that of a well developed, markedly cachectic white male (height 5 ft. 8 in., estimated weight 90 pounds). There was cyanosis of the nailbeds and slight clubbing of the fingers. There was a large tumor in the retropharyngeal space which extended from the oral pharynx through the nasopharynx and to the base of the skull. At that point it eroded the bone and invaded the posterior fossa in the midline just behind the dorsum sellae, invading and destroying the clivus. The tumor remained subdural. It was dark red, fleshy, soft and friable.

The heart was negative.

The major bronchi were filled with thick hemorrhagic, yellow streaked fluid. There was no lesion of the larynx, trachea or large bronchi. The visceral pleura of the right lung and the parietal pleura of both pleural cavities were studded with numerous small slightly elevated, firm yellow-white nodules. There was no fluid in either pleural cavity. A few fibrous adhesions were present in the right pleural cavity. The lungs were equal in size and each weighed 700 grams. The greater portion of the subapical region of the right upper lobe was occupied by a slightly nodular tumor measuring approximately 5 x 3 x 3 cm. (Fig. 3). It appeared to be intra-pulmonary and subpleural, its inner surface being flush with the inner aspect of the right upper lobe. It was completely enclosed within a capsule which separated it from the lung parenchyma. Upon careful dissection it became evident that the capsule was constituted by layers of visceral and parietal pleura (insert, Figure 3 and Figure 4A). Thus, the tumor was not intrapulmonary but was situated in the anterior mediastinum. It had formed an enclave in the inner aspect of the right upper lobe and had become molded to the deformed contour of the lung. The tumor, on section, was firm, yellow-white in color with numerous cystic spaces and hemorrhagic areas (Figure 4A). Throughout both lungs, there were numerous rounded, firm nodules varying in diameter from 0.5 to 2 cm. They were dark red and hemorrhagic with small areas of white tissue. These tumors, although spherical, were not encapsulated and merged with the surrounding parenchyma.

The tracheobronchial lymph nodes were increased in number and size. They contained nodules of yellow-gray tissue appearing to be metastatic tumor.

The liver weighed 1,250 grams and contained many nodules similar in size and

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Figure 5A: Hemangio-endothelioma, liver metastases. Fairly well defined vascular channels lined by prominent, hyperchromatic endothelial cells. Areas identical with these were present in the teratoma. (H&E x 200).—a: Silver reticulin stain of a comparable area. Intercommunicating vascular channels. Cells are situated within the reticulin fibers. (x 200).—*Figure 5B:* Hemangio-endothelioma, lung, metastases. Vascular channels obscured by many atypical and bizarre endothelial cells. Identical areas were present in the teratoma. (H&E x 200).—b: Silver reticulin stain of a comparable area reveals vascular pattern. (x 200).

appearance to those described in the lungs. The liver parenchyma was otherwise negative. The gall bladder and bile ducts showed no lesions.

In the right kidney, at the junction of medulla and cortex, there was a firm yellow-white nodule 1 cm. in diameter. The genito-urinary tract was negative.

Many sharply demarcated, punched-out, rounded lesions were found in a number of vertebra. Their appearance was similar to that of the pulmonary nodules.

The spleen, gastro-intestinal tract, pancreas, thyroid, brain and pituitary were negative.

Microscopic Examination: The mediastinal tumor was made up of a variety of elements including epithelial, glandular, vascular and connective tissue, arranged in a haphazard fashion (Figure 4A). The glandular elements consisted of irregular spaces with a variety of lining cells. Some were lined by columnar, mucin-secreting epithelium with basal nuclei suggesting intestinal epithelium. There were a number of markedly dilated glands filled with mucin and cellular debris (Figure 4C). Others were lined by ciliated epithelium of the respiratory type. Many glands were lined by flat or cuboidal cells which bore no distinct resemblance to differentiated structures. In some glands, the cells were heaped up and infiltrated the stroma. Nests of stratified epithelium were present and some exhibited keratotic pearl formation. A few cavities were lined by squamous epithelium (Figure 4C) and by nests of young nervous tissue. There were several foci of hyaline cartilage and a spicule of mature bone. The stroma was for the most part quite cellular and made up of fusiform cells with several prolongations. Small foci of embroyonal nonstriated muscle were present (Figure 4B). There were many hemorrhagic areas consisting of irregular vascular spaces filled with whole blood. Intercommunication between the vascular channels was frequent. These spaces were frequently lined by atypical endothelial cells which showed considerable variation in size and shape (Figure 5A and 5a). Many were elongated and flattened; others were quite large and projected into the lumen. The nuclei were generally small and hyperchromatic but they too showed considerable variation in size and shape. Many isolated bizarre tumor giant cells were interspersed among cells with huge multilobulated, hyperchromatic nuclei and multinucleated cells (Fig. 5B). Mitotic figures were not commonly observed. The vascular channels were, as a rule, lined by a single layer of endothelial cells. In some places, however, the cells were heaped-up, obliterating the lumen. In others, the endothelial lining was fragmentary and incomplete. There were many interlacing and intercommunicating cavernous, blood-filled spaces, separated by thin septa and lined here and there by a few flattened endothelial cells.

The tumor nodules in other sites were similar to the vascular portion of the mediastinal tumor. There was considerable variation in the histologic appearance of the nodules due to the varying degrees of prominence of the vascular channels and of the endothelial cells. Thus, in the retropharyngeal tumor there were large dilated, interlacing channels filled with blood and lined by discontinuous, bizarre endothelial cells. On the other hand, in the liver, the tumor was markedly cellular and the vascular channels were almost completely obliterated.

In other sites, the tumor nodules were composed of an admixture of hemorrhagic and cellular areas.

Almost all metastatic tumor nodules were characterized by some degree of hemorrhage, often very marked, which often extended into the surrounding tissue. Thus, the liver parenchyma and the pulmonary alveoli contained many large collections of erythrocytes, usually in the vicinity of the tumors.

The vascular component of the densely cellular areas was somewhat obliterated by the cellular growth (Figure 5B) but could be demonstrated with a silver reticulin stain. This revealed the characteristic, interlacing, irregular vascular channels with the cells lined up within the vessel wall (Figures 5A and 5B).

The nodule of the kidney was made up of spindle-shaped cells arranged in a faint whorling pattern. A few isolated, irregular tubular structures were present

within the framework of the nodule, a typical feature of benign fibroma of the kidney.[19]

Sections of lung taken from sites beyond the tumor nodules showed organizing pneumonitis and focal intra-alveolar hemorrhage.

The heart, gastro-intestinal tract, pancreas, adrenals, genito-urinary tract, thyroid, skin, muscle, pituitary and brain were negative.

Final Diagnoses:

1) Malignant teratoma (hemangio-endothelioma and adenocarcinoma) of anterior mediastinum, right;
2) Metastatic hemangio-endothelioma in lungs, parietal pleura, hilar lymph nodes, retropharynx, base of skull, vertebrae and liver;
3) Fibroma of kidney, right.

Comment

In the early phase of this patient's clinical course, the short history, bloody sputum, and pulmonary findings both on physical and x-ray film examinations, were suggestive of active pulmonary tuberculosis. Dissemination to the cervical and upper thoracic vertebrae was considered because of the complaints of pain in, and equivocal x-ray findings of these areas. However, even at this stage, it was noted that the x-ray films of the chest were somewhat unusual for tuberculosis. Head traction, applied for a short period of time, gave no relief from neck pain, and was then discontinued. After the first month of hospitalization, it was considered difficult to maintain the diagnosis of tuberculosis in view of the free bleeding without pus, and absence of positive sputa. Streptomycin and para-aminosalicylic acid were then discontinued. Although the mechanism of spread was not clear, the diagnosis of some variety of cancer (possibly lymphoma) was favored, and radiation therapy was started. During the latter part of the patient's course, the finding of a hard tender mass in the right nasopharynx dispelled any doubt that the problem was one of neoplasm rather than tuberculosis.

Mention should be made of the symptoms of cough, pain, hemoptysis and alteration of the voice. Here change in position neither precipitated nor alleviated the hacking cough. In the literature, blood streaked sputum in teratoma of the mediastinum is described as a terminal event. In this patient, the persistent bloody sputum, amounting to several ounces daily and leading to severe anemia, is considered unusual, and can be accounted for by the hemangiomatous pulmonary metastases. Pain in mediastinal teratomas has been described as pleuritic, anginal and occasionally abdominal. The pain in the neck and back in the case presented is atypical. The development of a nasal quality voice can be ascribed to the retropharyngeal mass rather than to recurrent laryngeal nerve involvement as frequently described.

It is of interest to note that there was no increase in size of the superior mediastinal shadow, and the pulmonary metastases were responsible for the patient's first symptoms. Cases similar to the one presented, where the first symptoms were due to metastases, are cited by Rusby.[4]

The density in the left upper lobe seen on x-ray inspection (Figure 1

and 2) was undoubtedly due to organizing pneumonitis and hemorrhage as well as small tumor metastases.

The location of the primary tumor was somewhat unusual. It was enclosed within the space formed by the mediastinal reflection of the parietal pleura. It undoubtedly arose within the superior and anterior mediastinum. The tumor shifted, however, to the inner aspect of the right upper lobe and there formed a deep depression (Figure 3). Possibly the pulsation of the aorta may have been a factor in the shifting and propulsion of the tumor.

Microscopically, the tumor showed fairly well defined organoid tissues derived from ectoderm, endoderm and mesoderm (Figure 4). Therefore, by definition it is a teratoma. The malignant component of the teratoma and its metastases present the two features which Stout[17] considers characteristic of hemandio-endothelioma. ("First, the formation of atypical endothelial cells in greater numbers than are required to line the vessel with a simple endothelial membrane, and, second, the formation of vascular tubes with a delicate framework of reticulin fibers and a marked tendency for their lumens to anastomose"—Stout[17]). The tumor shows many variations of these features which often tends to obscure its true nature. Many areas consist of anastomosing cavernous spaces in which areas reveal focal overgrowth of atypical endothelial cells. Conversely, there are areas in which there has been marked proliferation of atypical endothelial cells and the vascular feature is not evident with the hematoxylin and eosin stain. Here, a silver reticulin stain outlines the vascular channels and completes the picture. In this case, there was no question of multicentric origin, an issue which occasionally arises in considering these tumors (Jaffe[20]).

SUMMARY

A case of hemangio-endothelioma with many metastases arising from a mediastinal teratoma is presented. The rarity of this tumor, its unusual anatomic location and the relevent clinical features, on the basis of which the diagnosis might have been suspected, are discussed.

RESUMEN

Un caso de hemangio-endotelioma con muchas metástasis emergiendo del teratoma mediastinal es presentado. Se discute la rareza de este tumor, su extraña situación anatómica y sus relevantes características clínicas, en cuyas bases el diagnóstico pudo ser adivinado.

RESUME

Les auteurs présentent un cas d'hémangio-endothéliome avec nombreuses métastases provenant d'un tératome médiastinal. Ils exposent quelques considérations sur sa localisation anatomique inhabituelle, et les éléments cliniques essentiels sur lesquels il convient d'établir les bases du diagnostic.

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Esophageal Carcinoma with Alveolar Cell Tumor of the Lung*

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Interest in the recent literature on alveolar cell tumors of the lung has centered about the disagreement as to their histogenesis. With regard to their development from the alveolar lining, Bensley and Bensley[1] believe that a continuous layer of epithelial cells line the alveoli. Others feel that the alveoli have a discontinuous epithelial lining, and some think that no true epithelial lining of the alveoli exists. These different views have been well summarized by Neubeurger and Geever.[2] However, studies of the lung under inflammatory conditions and in chronic passive hyperemia have demonstrated what is considered by many to be epithelial proliferation from alveolar lining cells.[3,4] It would therefore appear valid to state that under certain pathologic conditions and possibly normally, the alveoli have a definite epithelial lining. An origin of these tumors from bronchiolar epithelium has been suggested by Herbut,[5,6] but this concept has not been substantiated by actual gross or microscopic examinations. Finally, a metastatic origin has been considered. Neubuerger and Geever[2] state that by definition primary cancer elsewhere in the body must be excluded. Others[7] have also emphasized this point among the criteria for diagnosis.

The following case, believed to be the first to illustrate such a coincidence of an alveolar cell tumor and primary carcinoma elsewhere, is being reported to demonstrate that the presence of another malignancy does not invalidate the diagnosis of primary alveolar cell tumor of the lung. Wood and Pierson[8] reported a case in which the pulmonary lesion was diagnosed by lobectomy and the patient, while under observation developed an adenoacanthoma of the cervix.

Case Report

M. B., a 57 year old colored female was admitted to Gallinger Municipal Hospital, Washington, D. C., on January 18, 1949 with the chief complaints of dyspnea and fatigue. She had episodes of generalized weakness and fatigue requiring bed rest at sporadic intervals for the previous four years. Approximately six weeks prior to admission the patient developed a "weak spell" in association with cough productive of moderate amounts of white sputum. Also during this time she estimated a weight loss of 30 pounds and for several days prior to admission dyspnea had been present. Past medical history and systemic inquiry were not informative. On physical examination the patient showed signs of recent weight loss and was dyspneic even at rest. Masses of matted supraclavicular nodes were present, there were signs of fluid over the right hemithorax and diffuse moist rales were heard over the entire left chest.

The admission blood count was essentially normal. The urine was normal and the serologic tests for syphilis were negative. A chest x-ray film showed right

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pleural effusion and miliary mottling was present throughout the left lung (Figure 1). Findings were intrepreted as being consistent with miliary tuberculosis with right pleural effusion. Repeated sputum studies and bone marrow examinations were negative for acid fast bacilli. Right thoracentesis was done and 1,000 cc. of orange-red fluid were removed. A chest x-ray film after this procedure showed miliary mottling on the right. A cell block from the pleural fluid showed cells suggestive of neoplasm. Biopsy of a right supraclavicular node showed papillary adenocarcinoma, metastatic, possibly of overian origin. A low grade fever was present during the period of hospitalization. Despite supportive therapy she expired on April 8, 1949.

At autopsy both lungs were studded with white rubbery nodules varying in diameter from 0.5 to 1.5 cm. (Figure 2). The right pleural space contained approximately 2,000 cc. of greenish pleural fluid. The left pleural space was obliterated by adhesions. Many of the mediastinal nodes were replaced with firm white areas similar to those found in the lung. The deep lymph nodes of the anterior cervical region showed similar changes. The liver and spleen contained nodules like those found in the lung. The lower third of the esophagus in its posterior portion had a mucosal ulceration approximately 2.5 cm. in diameter. The lung sections on microscopy showed the alveoli to be lined by neoplastic cells with hyperchromatic nuclei. The alveolar septa were not appreciably thickened and minimal inflammatory cell infiltration was noted (Figure 3). The metastatic areas which were present in the mediastinal and cervical nodes, liver, spleen, thyroid and adrenals were similar to the pulmonary lesion. The esophageal lesion was a typical squamous cell carcinoma (Figure 4).

Comment

A recent paper by Good et al.[9] from the Mayo Clinic has done much to clarify some of the confusion about these tumors. These authors divide them into grades 1 to 4. Those cases showing the most regular cells with the smallest nuclei are placed in grade 1 while those with the largest

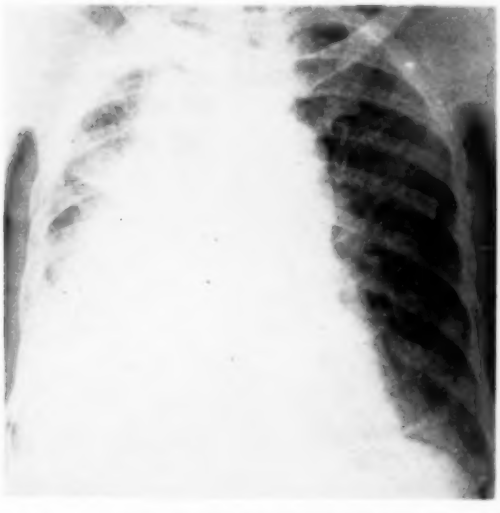

FIGURE 1: From chest x-ray film showing miliary mottling of left lung field and right pleural effusion.

nuclei and the least regular cells are placed in grade 4. Grade 4 tumors are the ones which may show distant metastases. They also state that the cases in grade 1 may belong to the group called pulmonary adenomatosis. Definite histopathologic criteria have also been established for making the diagnosis of alveolar cell tumor of the lung. The alveoli should be lined by columnar cells which may show various grades of malignancy and may also be formed into papillary projections. Further the inter-

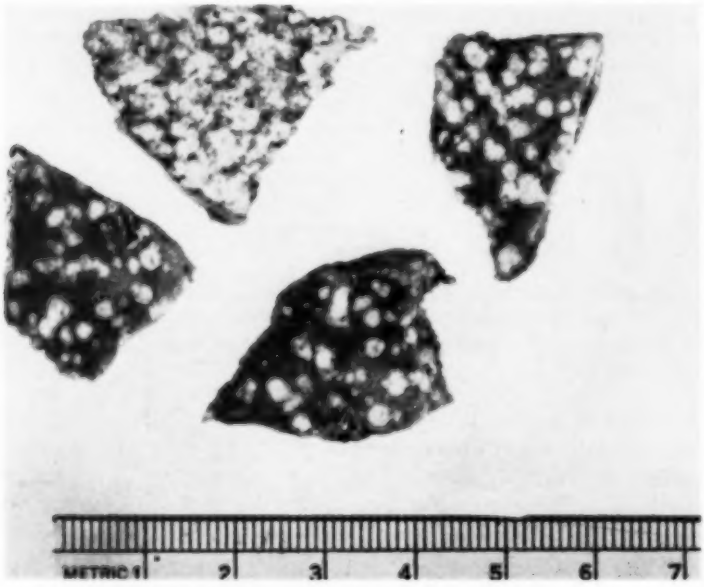

FIGURE 2: Gross appearance of lung lesions.

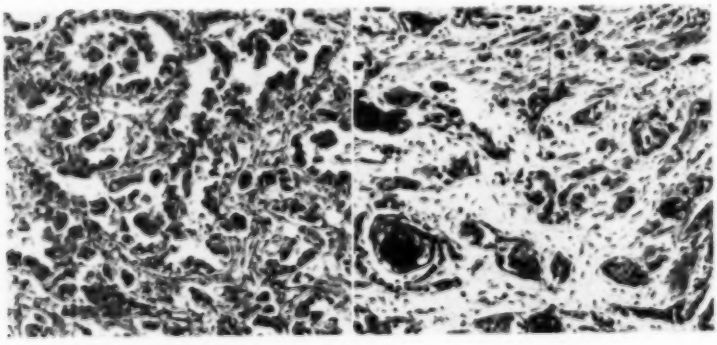

FIGURE 3 FIGURE 4

Figure 3: Photomicrograph showing the alveolar cell tumor pattern. Hematoxylin and eosin. (x 180). — *Figure 4:* Photomicrograph of esophageal squamous cell carcinoma. Hematoxylin and eosin. (x 180).

alveolar septa should be thickened slightly or not at all and there should be little evidence of an inflammatory reaction. It is believed that if these criteria are followed the question of metastatic malignancy need not be a problem. It is therefore demonstrated by this case that the diagnosis of alveolar cell tumor should be made on its own merits and the absence of a primary cancer elsewhere is not a requisite for making this diagnosis.

Another interesting feature of this tumor is its morphologic similarity to lesions found in sheep, mice, horses and guinea pigs. This disease has been called jagziekte, pulmonary adenomatosis and infectious adenomatosis. The exact cause of this disease is unknown but it is believed to be infectious and possibly viral in origin. There is no characteristic clinical picture although the most common symptoms are cough productive of sputum, dyspnea and hemoptysis. However, a typical type of sputum may be present in approximately 32 per cent of cases.[10] This is a profuse watery mucoid sputum which may exceed 1,500 cc. per day. It is possible for the quantity of the sputum to be so great as to cause electrolyte depletion.[11] The x-ray findings are not typical although alveolar cell tumors should be considered in the differential diagnosis of diffuse bilateral involvement. Probably the most valuable aid in the diagnosis is cytologic examination of the sputum or bronchial secretions.[9,11] Good et al[9] state that the only effective treatment is excisional therapy and that two of nine patients on whom this type of surgery was performed are alive and well after five years. They also note that another possible therapeutic approach which should be explored is a combination of surgery and irradiation.

SUMMARY

A case, believed to be unique, of alveolar cell tumor of the lung in association with squamous cell carcinoma of the esophagus is presented.

It is believed that the absence of a primary cancer elsewhere should not be one of the criteria for making the diagnosis of alveolar cell tumor of the lung.

Acknowledgment: I wish to thank the following for their help in the preparation of this paper: Dr. R. A. Kern, Dr. J. R. McDonald of the Mayo Clinic for reviewing the microscopic sections and Dr. E. S. Gault of the Pathology Department of Temple University Medical School who took the photomicrographs.

RESUMEN

Se presenta un caso, que se cree único, de un tumor pulmonar de células alveolares acompañado de un carcinoma del esófago de células pavimentosas.

Se opina que la ausencia de una cáncer primario en otra region no debe ser requisito para hacer el diagnóstico de tumor pulmonar de células alveolares.

RESUME

L'auteur rapporte l'observation qu'il pense être unique d'un cancer alvéolaire du poumon associé à un cancer de l'oesophage.

Il pense que l'absence de cancer primitif sur un autre viscère ne doit pas être un des arguments sur lesquels on se base pour poser le diagnostic de cancer du poumon à cellules alvéolaires.

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A Report on the Use of Carbarsone in Pulmonary Tuberculosis*

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Carbarsone is an arsenic compound and has been used for a number of years in the treatment of amebic dysentery. It is the trade name for p-carbamino phenyl-arsonic acid ($H_2O_3As.C_6H_4NHCONH_2$) which was first prepared by Ehrlich. It is a white, crystalline, odorless solid, stable in air, with a slightly acid taste, and is practically insoluble in water, but is soluble in carbonate or bicarbonate solutions.

Our interest in the use of carbarsone in the treatment of tuberculosis was stimulated by the work of Dr. Robert Siver of Baltimore, Maryland, who had been using carbasone in the treatment of various forms of the disease. His results were far from conclusive, but several patients were apparently improved, and in February 1950 before a Regional Meeting of the American College of Physicians, he reported that the drug had a retarding effect on experimental tuberculosis in guinea pigs as well as in human tuberculosis. We, therefore, decided to try carbarsone on a limited number of patients at Eudowood Sanatorium to determine whether this drug had any effect on clinical tuberculosis. The therapeutic program was the same as that outlined by Dr. Silver and was continued for a period of at least three months. This therapy consisted of:

(1) Carbarsone $3\frac{3}{4}$ grains—twice daily for five days.
(2) Sulfadiazine $7\frac{1}{2}$ grains—four times a day for five days.
(3) Ten days rest without medication.
(4) Carbarsone $3\frac{3}{4}$ grains—twice daily and sulfadiazine $7\frac{1}{2}$ grains—four times daily for five days in combination, followed by ten days rest. This last medication was repeated over and over during the entire therapeutic trial.

Before treatment the following procedures were carried out, complete blood count, sedimentation rate and sputum examinations, including sensitivity of organisms to streptomycin when streptomycin had been used previously. These were repeated at six week intervals. X-ray films were taken before treatment and at 30 day intervals thereafter. The clinical condition of the patient was checked at two week intervals, particularly concerning cough, expectoration, weight, etc.

Clinical Trial of Carbarsone on Pulmonary Tuberculosis

Thirty patients with pulmonary tuberculosis were placed on carbarsone therapy for a period of at least three months and several as long as six months. The cases treated were classified as predominately exudative or productive. Practically all cases were far advanced with a poor prognosis so that no unusual results were anticipated, but it was our desire to observe

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any tendency toward improvement in order to determine whether further and more extensive clinical trials would be advisable. Cases were divided into predominately exudative and predominately productive lesions.

Cases with predominately exudative lesions:

There were only three cases which might be classified as exudative. One had a pneumonic involvement which showed some clearing of disease and improvement, one was stationary and one had an acute exascerbation while on carbarsone. This latter case was treated with carbarsone before admission to the sanatorium.

Cases with predominately productive lesions:

Ten were worse, 16 were stationary and one was improved. Of those that were worse, five had streptomycin and para aminosalicylic acid after discontinuing carbarsone—all of these cases were improved on streptomycin and para aminosalicylic acid therapy.

Only one case of tuberculosis of the kidneys received carbarsone for two months. At the end of this trial period, the patient was unimproved clinically. This patient was placed on streptomycin and para aminosalicylic acid after discontinuing carbarsone, and showed considerable symptomatic improvement after two months treatment.

Results

There were only two patients of the entire group who seemed to be improved while on carbarsone, but this improvement was far from impressive. The rest were either stationary or worse. The group studied was too small to form any conclusion, but it was our impression that in these cases the disease seemed to run its natural course without any beneficial effects noted. Several who received carbarsone before any other antibiotic, were either stationary or worse, whereas, these same patients unmistakedly improved when placed on streptomycin and para aminosalicylic acid.

X-Ray Analysis

From the x-ray film appearance 14 were considered stationary, 14 worse, one slightly improved and one moderately improved while on carbarsone.

Of the entire group only two patients felt generally better, but there was no evidence of improvement in x-ray film or laboratory findings.

There was no toxic manifestation noted except a skin rash in one patient, and it was doubtful if this was due to the medication. The drug was discontinued because she had received it for over three months and had done poorly. She died several weeks later.

There seemed to be a tendency in about one-half of the patients to have an increase in cough and expectoration for several weeks after the drug was begun, and thereafter they continued at the pretreatment level. Only one had conversion of sputum from positive to negative during the course of treatment.

Seven showed gain in weight of from two to 14 pounds, while 16 lost from one to eight pounds and six maintained their weight.

In all patients with fever, little or no change in temperature took place. In one, there was an elevation to 103 degrees F., due to acute exascerbation of the disease while still on the drug.

There was no change in the hemoglobin, red blood count or white blood count in any case.

Two patients showed improvement in sedimentation rate "Cutler method" (a drop of 5 mm. per hour). Six were worse (an increase of 5 mm. or more per hour). Twenty-one were stationary.

Resistance to streptomycin: There was no change in sensitivity to tubercle bacilli to streptomycin in several patients on whom streptomycin sensitivity tests were run before and after carbarsone therapy.

Case Report

The following is an example of the Predominately Exudative Type: Carbarsone—From March 21, 1950 to August 11, 1950.

This patient, W.P., a 49 year old, white male, was admitted to Eudowood Sanatorium February 9, 1950. Onset, with fatigue and loss of weight of two years duration. X-ray film, one month before admission, revealed evidence of disease which proved to be active pulmonary tuberculosis. On admission, he had an area of consolidation in the right lung above the third rib. His temperature was 100 degrees F. Sputum positive for tubercle bacilli. He was started on streptomycin (one-half gram twice a day) February 10, 1950, and discontinued May 8, 1950. His temperature had gradually come down to 99.2 degrees F., but this change occurred before carbarsone therapy. He has gained 14 pounds in weight while on carbarsone, and the disease has gradually cleared although he still has a positive sputum. His sedimentation rate has dropped from 26 before therapy, to 18 at the end of carbarsone. He has improved about as one would have expected from his streptomycin therapy and bed rest. There has been no additional improvement that one could attribute to carbarsone. Surgery is being contemplated.

Since concluding our clinical observation on carbarsone, we have received a report from Dr. J. W. Frost of the Lilly Research Laboratories on carbarsone therapy in human and animal experiments. He states that

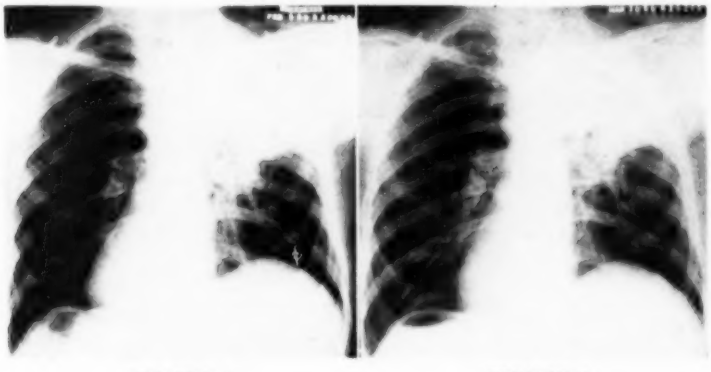

FIGURE 1 FIGURE 2

Figure 1: Admission film. Consolidation right upper.
Figure 2: Before Carbarsone. No changes from admission film.

FIGURE 3 FIGURE 4

Figure 3: Little or no clearing after Carbarsone.
Figure 4: Considerable clearing since July 27, 1950, with no drug therapy. Surgery contemplated.

several patients studied at the Lilly Laboratories for Clinical Research, showed no clinical response, and, likewise, animal work showed evidence that the material did not have any effect on experimental tuberculosis in mice or guinea pigs.

SUMMARY

Clinical observations on 30 cases on carbarsone showed no evidence of any effect of this drug on pulmonary tuberculosis or one case of renal tuberculosis. Unless evidence can be obtained to show a retarding effect of carbarsone on experimental tuberculosis further clinical trials are not warranted in our opinion.

RESUMEN

Las observaciones clinicas en 30 casos tratados con carbarzona no mostraron evidencia alguna de efecto sobre la tuberculosis pulmonar ni tampoco en un caso de tuberculosis renal. A menos que se obtenga evidencia de un efecto retardante de la carbarzona en la tuberculosis experimental, no estan justificados nuevos ensayos clinicos en nuestra opinion.

RESUME

Les observations cliniques de 30 malades traités par le carbazone n'ont montré aucun effet net sur la tuberculose pulmonaire et dans un cas sur une localisation rénale. Ce n'est que si les travaux expérimentaux permettent d'obtenir un effet retardant sur l'évolution de la tuberculose que de nouveaux essais cliniques avec ce produit se montreraient nécessaires.

Kymography of Diaphragm*

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History: In 1901 Ejkmann[1] introduced the roentgen-cinematographic study of some organs; but it is Bronislaw Sabat, a physiologist of Warsaw (Poland), who is to be credited for roentgen-kymography. He divised, in 1911, the recording procedure of the movement of internal organs by means of x-rays, using a simple slit made in a sheet of lead. One year later, Gott and Rosenthal[2] emphasized its possible clinical value. In 1915, A. W. Crane,[3] presented for the first time in the United States of America, the foundations of roentgen-kymography. Stumpf of Munich (Germany), not only perfected the apparatus already known and developed his roentgen-kymograph used at the present time, but he reported the results of his experiments about recording, by means of waves, the movements of almost all internal organs.

Mechanics of Roentgen - Kymography: Etymologically *"kymography"* means *"recording of waves."* To such purpose, there are available two systems of apparatus; one in which the lead grid is moved; and the other in which the grid is stationary while the x-ray film is moved.

We shall assume for instance that, in Figure 1, the grid is moving upwards. *Pb* are lead sheets and *A* is a slit or small window free of lead. In the position of Figure 1, behind the slit at the moment of recording, we assume that a segment of heart is in systole, represented by notches *5* and *6*. As only this heart segment is in front of the window free of lead, *only such segment* will record its figure by the action of x-rays.

At the moment represented by Figure 2, as the grid has been moved upwards, the myocardial segment *5* and *6* has been covered by the lead.

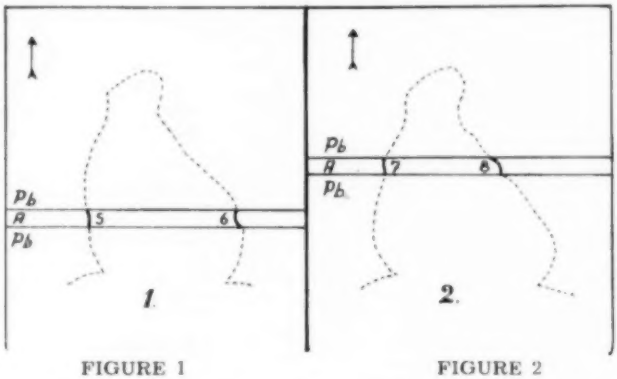

FIGURE 1 FIGURE 2

*Presented at the Sixth International Congress of Radiology, London, England, July 23-28, 1950, and read at Church House on July 25.

and other segments *7* and *8* has occupied the window place; but as the moments are different, the heart instead of being in systole is in diastole, which we represent with the salients *7* and *8* as a salient. Thus we shall obtain the *kymographic wave* in the shape of an indented line.

The Diaphragm: Located between the thoracic and abdominal cavities, it presents two aspects: an upper or convex surface, and a lower or hollow one. The former, in its central portion, corresponds to the pericardium and heart. The pericardium is situated on the anterior part of phrenic center which, as it is well known, is of a tendinous structure, very strong and tough. The pericardium is attached to the diaphragm to give it the upper point of fixation, which is the only one the muscle has on its convex surface.

Radiographic Technic: We have been unable to secure accurate data about the technic for securing kymographic films of diaphragm.[6,7] The technic below has been devised by the author.

For Frontal Kymography:

Penetration	75 to 80 KV.
Milliamperes	100 milliamperes (rotating anode)
Distance	120 cm.
Exposure time	5 seconds.

For Lateral Kymography:

Penetration	80 KV.
Milliamperes	100 milliamperes (rotating anode)
Distance	92 cm.
Exposure time	5 seconds.

Apparatus used: Fluoradex D-500 milliamperes, rotating anode tube, Westinghouse; kymograph of stationary grid Liebel-Flarsheim, of Cincinati, Ohio.

Position of Kymograph: For frontal kymograph: blind with vertical bands. For lateral kymography: blind with horizontal bands.

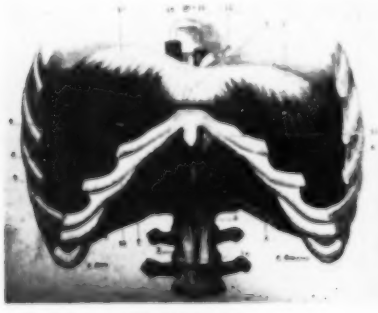

FIGURE 3

FIGURE 4

Figure 3: Diaphragm viewed from above (Testut).
Figure 4: Structure of diaphragm (Testut), same surface.

SUMMARY

The history of the roentgen-kimographic procedure in the study of the diaphragm, and its importance, is emphasized as an air for diagnosis; its physical basis is reviewed, and the manner of obtaining the waves is explained; the correlation of anatomy and kimographic findings is discussed.

The technique and a series of cases are presented, starting with those obtained in normal individuals. In each case a description of the pneumopathy is given. Complete details referring to radiographic technique, are presented.

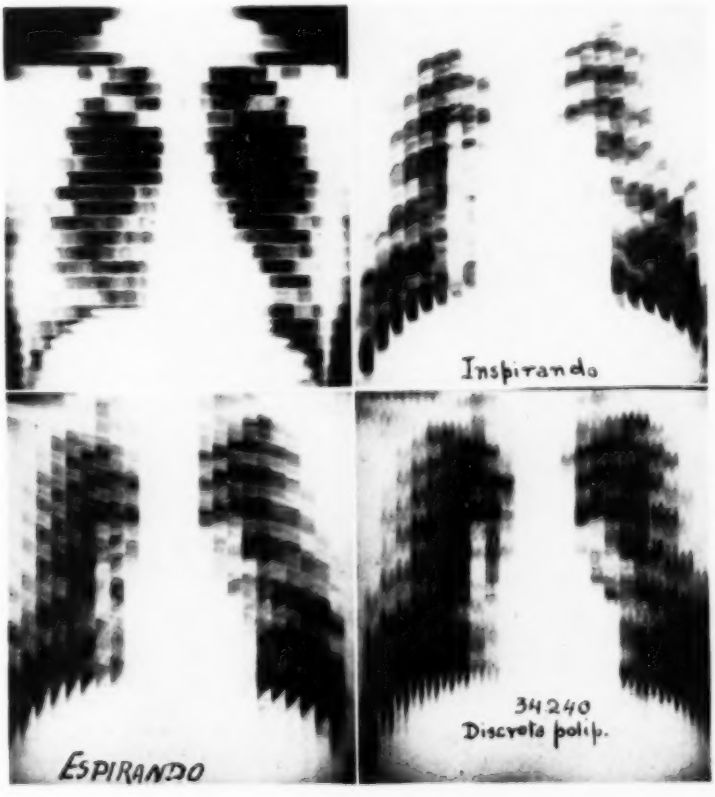

Figure 5 (upper left): Kymography of heart without apnea. Diaphragmatic waves can be differentiated in a horizontal direction.—*Figure 6 (upper right):* Kymography of diaphragm during inspiration. Half waves located at the right of the grid can be viewed.—*Figure 7 (lower left):* Kymograph of diaphragm during expiration. As in the former case, half waves can be viewed, but this time located at the left of the grid.—*Figure 8 (lower right):* Kymograph of diaphragm in discreet polypnea. Complete waves of diaphragm are registered tooth-shaped in a vertical direction.

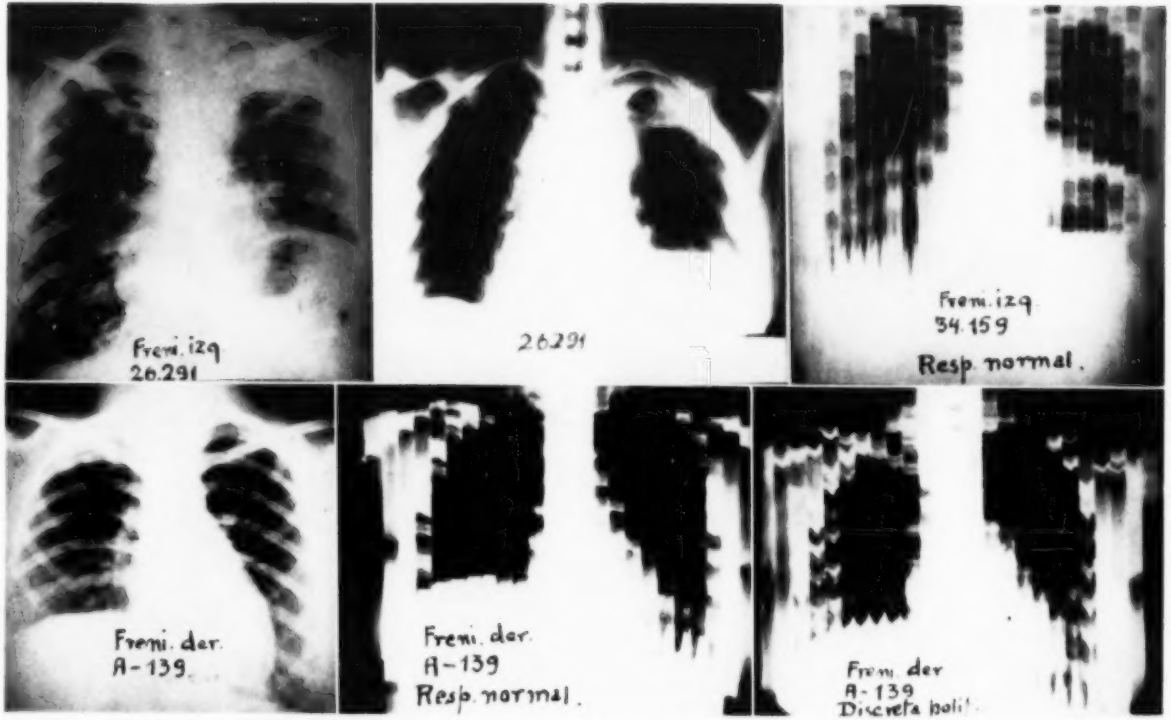

Figure 13 (upper left): Left phrenicectomy done 11 years before.—*Figure 14 (upper middle):* Tomography of the former case at 8 cm. of posterior wall of thorax—*Figure 15 (upper right):* Kymograph in frontal projection. Absence of waves in the operated hemidiaphragm.—*Figure 16 (lower left):* Right phrenicectomy done four years before.—*Figure 17 (lower middle):* Kymography of the former case in normal respiration. "Plateau" appearance of right hemidiaphragm.—*Figure 18 (lower right):* Kymography of same case in forced inspiration. Very small waves of a dicrotic type, on the right side.

RESUMEN

En este trabajo se revisa la historia del procedimiento roentgenkimográfico aplicado al diafragma, recalcándose su importancia como elemento de diagnóstico; se repasa sus fundamentos físicos y se explica la manera cómo son obtenidas las ondas; se recuerda la anatomía y fisiología del músculo diafragma con el objeto de relacionarlo con la kimografía; se pone al alcance de los lectores detalles completos en lo concerniente a técnica radiográfica; en fin, se pone a disposición de los aficionados nutrida iconografía de casos, empezando con trazados de individuos normales. En cada caso se da la correspondiente leyenda de acuerdo con la neumopatía causante de la alteración. Se acompaña la necesaria bibliografía.

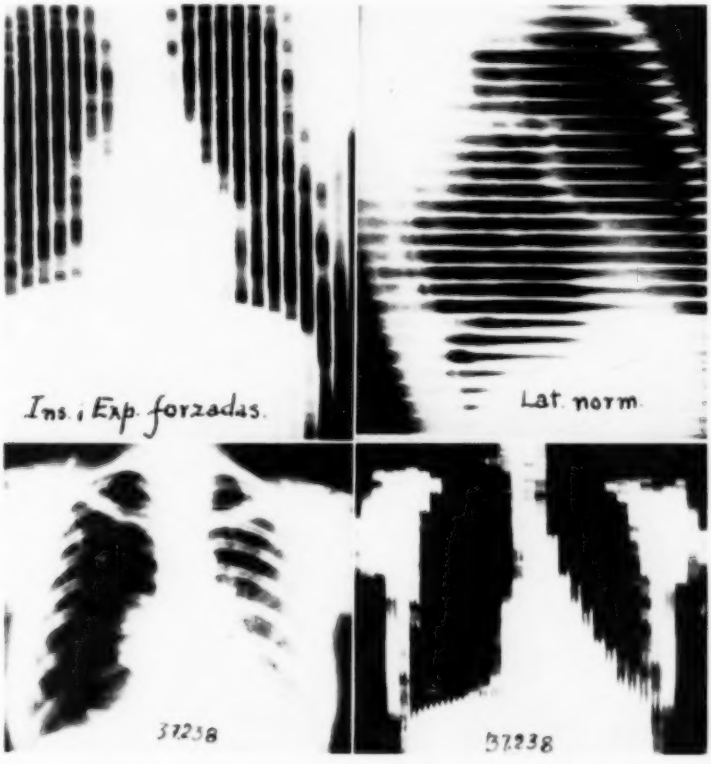

Figure 9 (upper left): Kymograph of diaphragm in forced inspiration or expiration. Absence of waves in such a way that diaphragmatic figure is shown in "plateau."—*Figure 10 (upper right):* Kymograph of diaphragm in lateral right. Waves of halves anterior and posterior of diaphragm are very unequal; waves of posterior half have an exceptional amplitude, larger than those of anterior segment.—*Figure 11 (lower left):* Right therapeutic pneumothorax.—*Figure 12 (lower right):* Kymography of former case. The waves of hemidiaphragm of pneumothorax side are smaller than those of the opposite hemidiaphragm and very lightly dicrotic.

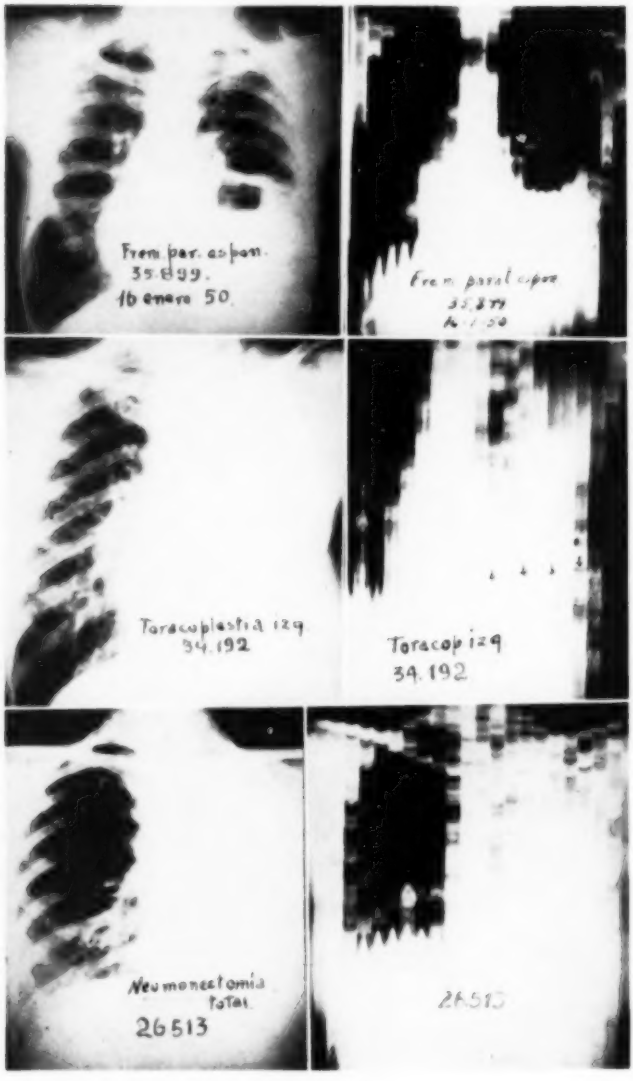

Figure 19 (upper left): Spontaneous phrenic-paralysis on the left side, disclosed five years before.—*Figure 20 (upper right):* Kymograph of former case in frontal projection. Absence of waves on side affected.—*Figure 21 (middle left):* Left nine-rib thoracoplasty.—*Figure 22 (middle right):* Kymograph of latter case. Waves of left hemidiaphragm are absent (the arrows, in the original, show the direction of the organ).—*Figure 23 (lower left):* Total left pneumonectomy for tuberculosis.—*Figure 24 (lower right):* Kymography in frontal of latter case. Absence of waves in the diaphragm of the operated side.

RESUME

L'auteur considère comme une aide importante pour le diagnostic l'étude radio-kimographique du diaphragme. Il développe son historique et son importance. Il passe en revue ses bases physiques et la façon d'obtenir les courbes. Il discute les rapports des constatations kimographiques et de l'état anatomique.

Il décrit la technique et rapporte une série d'observations en commençant par celles qui ont trait à des individus normaux. Dans chaque cas, il précise les caractères de la pneumopathie. Il y associe tous les détails concernant la technique de la radiographie.

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Diagnosis and Management of Esophageal Hiatus Hernia*

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Herniation of a portion of the stomach into the chest through the esophageal hiatus of the diaphragm is the most common type of diaphragmatic hernia. Harrington has stated that 95 per cent of diaphragmatic hernias in the adult are of this type. The fluoroscopic and x-ray study furnishes the basis for the diagnosis. It was only after the roentgen method of diagnosis became well developed and universally applied that the true incidence of this type of hernia became evident.

The Symptoms

Though it is possible for the patient with an esophageal hiatus hernia to have no symptoms from the hernia in my own experience the majority have a variety of symptoms which may be grouped as follows:

1) Symptoms suggestive of gastrointestinal disease.
2) Symptoms of acute gastrointestinal hemorrhage with hematemesis, melena or both.
3) Symptoms due to chronic blood loss.
4) Pain similar to that seen in angina pectoris and closely resembling myocardial infarction.

A combination of the above symptoms may occur in an individual patient.

Discussion of Symptoms

1) The most common symptom may be described as "indigestion" consisting of epigastric pain or discomfort related to meals, and relieved by factors which apparently decrease the size of the hernia. The occurrence of pain soon after meals makes the patient afraid to eat. The act of vomiting, eructation of gas, or the ingestion of alkali may relieve the pain. Small meals or the eating of meals in an erect position may prevent the onset of pain.

The mechanism of the production of the pain is uncertain. The pain may be associated with overdistension of the herniated portion of the stomach by ingested food or gas. Cholecystitis with or without cholelithiasis, not uncommonly occurs with hiatus hernia and may play some part in the production of pain. Peptic ulcer in the lower esophagus or in the abdominal portion of stomach or duodenum may be present simultaneously with hiatus hernia and cause pain.

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2) Acute blood loss, as evidenced by hematemesis or melena, may be the first indication of the existence of hiatus hernia. The differentiation of this type of hemorrhage from other causes of upper gastrointestinal bleeding is difficult without x-ray studies.

3) In some patients fatigue and weakness may be the symptoms that bring the patient to the physician. Anemia may be discovered on routine study. The presence of occult blood in the evacuations may indicate that the cause of the anemia is due to intestinal bleeding. The site of bleeding may be from an ulcer in the hiatus hernia or from erosion of the mucous membrane of the stomach at the point of constriction by the diaphragm.

4) Esophageal hiatus hernia may produce symptoms which may be confused with those due to serious heart disease. Substernal distress occasionally radiating to the left shoulder and down the arm into the little and ring fingers, are encountered occasionally in the patient with esophageal hiatus hernia.

Although exertion frequently precipitates substernal pain in the patient with such a hernia, it rarely does so consistently. Dietary indiscretions and nervous tension usually precipitate attacks of pain or discomfort. A large meal or the injudicious use of alcohol frequently cause symptoms, particularly in the presence of emotional disturbances. Nocturnal attacks when the patient is in a recumbent position are not uncommon. A close relationship between the onset of symptoms and the act of lying down or bending forward has been stressed by most observers. A further difference between the patient with the hernia and those suffering from angina pectoris lies in the frequent and striking relief the patient with a hernia obtains by the use of atropine. Although nitroglycerin affords dramatic relief from pain in some patients, it frequently fails.

The associated general symptoms and signs of acute peripheral vascular failure may be present in both conditions. In some of the cases of hiatus hernia the pain is relieved by vomiting or belching. The absence of physical signs such as a falling blood pressure, pericardial rub, gallop rhythm and arrhythmias does not exclude myocardial infarction.

Diagnosis

Fluoroscopic and roentgenographic studies are essential for the diagnosis of esophageal hiatus hernia. These examinations determine the type of hernia, the size of the hernia, the presence or absence of complications, such as ulcer. The examination will also help to rule out cardiospasm, esophageal diverticula and the phrenic ampulla. Other possible concomittant gastrointestinal diseases such as cholelithiasis, peptic ulcer and colonic diverticula must be identified if present. In the sliding type of hernia examination in the Trendelenburg position is important. The ordinary barium mixture is given by mouth and placed in a Trendelenburg position. He is instructed to take a deep breath, to hold the breath and then to bear down as though making the bowels move. This maneuver of valsalva helps to demonstrate the small esophageal hiatus hernia. The patient should also be studied in the standing position to determine if

the hernia moves down into the abdominal cavity or remains fixed above the diaphragm.

It is necessary to determine the position of the esophagus to differentiate the congenital short esophagus with thoracic stomach from the true hernia. At times this differentiation is almost impossible except by esophagoscopy and biopsy.

Esophagoscopy is indicated to determine the presence of a peptic ulcer or erosion in the esophagus or within the hernia in cases of hemorrhage and chronic blood loss. It is also helpful to obtain a biopsy specimen of the mucosa to determine if gastric tissue is actually present in the hernia, to establish the diagnosis of a congenital short esophagus.

The presence of a hiatus hernia may occasionally be suggested on an ordinary postero-anterior film of the chest. A shadow behind the heart or a gas bubble above the diaphragm may be seen. Confirmatory evidence of the presence of the hernia must, however, depend on barium meal studies.

A white female, age 42, had hypochromic microcytic anemia of unexplained origin. She also had had bloating and epigastric discomfort for sometime and occasional substernal oppression with difficulty in breathing. Examination of the heart revealed no organic disease. A large rounded gas bubble above the diaphragm was seen by the cardiac consultant who suspected esophageal hernia. A large esophageal hiatus hernia was readily demonstrated by fluoroscopy and roentgenography (Figure 1).

A white male, age 77, had attacks of dizziness and weakness for many years. An esophageal hiatus hernia, esophageal diverticulum and colonic diverticula were found by x-ray study (Figure 2). The attacks were accompanied by marked bradycardia. This was thought to be due to irritation of the vagus nerve by the diverticulum. Atropine sulphate gr. 1/75th t.i.d. abolished this vago-vagal reflex. The cardiac studies were normal. He had occasional severe attacks of substernal pain which closely resembled myocardial infarction. The pain necessitated repeated injections of opiates for relief. These attacks were thought to be due to incarceration of the esophageal hernia. Surgery was refused.

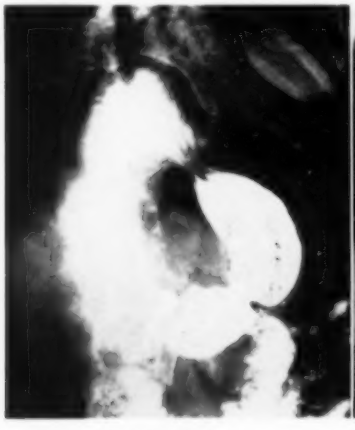

FIGURE 1

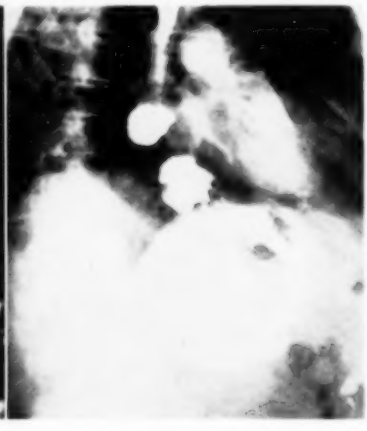

FIGURE 2

A white female patient, age 55, complained of gas all the time with pain in the left upper abdomen and a sore spot in the right shoulder blade. She also had heartburn, bloating and attacks of vomiting with occasional shortness of breath. Her cardiac examination was normal. The blood pressure was 130/80. She was worried only about heart disease. Fluoroscopic and roentgenographic studies revealed a diverticulum of the esophagus and an esophageal hiatus hernia (Fig. 3).

A white female patient, age 77, had difficulty in swallowing. She vomited if food was taken too fast. She had substernal discomfort. A fluoroscopic and roentgenogram study revealed a large esophageal hiatus hernia (Figure 4).

A white female patient, age 30, complained of tightness in chest and occasional difficulty in swallowing. The roentgenograms and fluoroscopy demonstrated a phrenic ampulla (Figure 5).

A white male patient, age 65, complained that food did not go through when he swallowed. He was bloated and gassy. The heart was normal. An esophageal hiatus hernia was demonstrated by x-ray study (Figure 6).

FIGURE 3

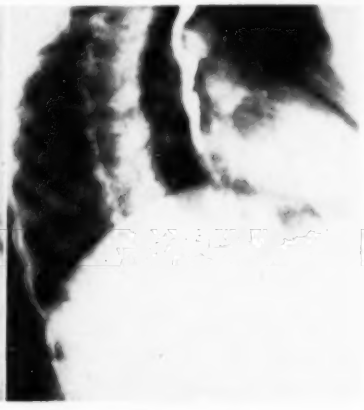

FIGURE 4

FIGURE 5

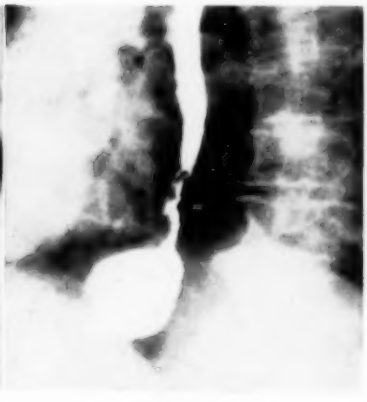

FIGURE 6

Discussion

It is still not too well known that substernal pain radiating into the shoulder or arm may be caused by stimuli arising elsewhere than in the heart. Patients are seen who have been given a doubtful or rather gloomy prognosis in whom an adequate examination reveals little or no evidence of heart disease. Anginal pain wholly comparable to that originally described by Heberden can be due entirely to other than cardiac causes. It is important to recognize the frequency with which such conditions simulate the typical pain of angina pectoris.

Several observers have pointed out the relative frequency with which small hiatus hernias cause substernal pain. It is important to note that anginal pain may be due to a small hiatus hernia even in the presence of coronary disease. The hernia may act as a trigger mechanism to set off the attacks. Adequate treatment of the hiatus hernia may prevent the attacks.

A variety of explanations have been offered for the pain associated with these hernias. Numerous authors have attributed dyspnea, palpitation and cyanosis, as well as the sensation of tightness in the chest, to actual displacement of the heart and mediastinal organs by the contents of the hernial sac. Such an explanation is reasonable when the hernia is large and contains a major portion of the stomach or other abdominal viscera.

Aside from the effects of displacement of the mediastinum, any attempt to explain the symptoms of esophageal hiatus hernia must be based on a consideration of the sensory pathways included in the trunks of the vague and phrenic nerves and in the afferent neurones of the upper thoracic trunks.

Von Bergmann, in 1932, after a careful investigation of what he termed the "gastrocardiac complex," was convinced that the cardiac symptoms associated with diaphragmatic hernia were due to pressure on the vagus fibers, with consequent reflex disturbances of the coronary circulation.

Jackson and Jackson attempted to prove that the pain of angina pectoris was not directly related to the heart. They believed that air or other stomach contents became trapped in the stomach or the esophagus, with resulting anginal pain. They attributed this to acute spasmodic, uncoordinated contractions of the esophagus and stomach.

Morrison and Swalm reported definite cardiac disturbances as indicated by electrocardiographic changes following balloon distention of the esophagus in patients with organic heart disease. These observations were made on patients suffering from typical anginal pain associated with heart disease, and proved that pain caused by intracardiac disease may be initiated by distention of the esophagus.

That esophageal or gastric disturbances may be responsible for widespread vagal stimulation with resulting bradycardia finds ample confirmation in clinical literature and in bedside observations. That such a phenomenon in the absence of heart disease is responsible for reflex coronary constriction, which results in anginal pain in patients with diaphragmatic hernia, is more difficult to believe.

Jones, after careful studies stated that the anginal pain experienced by patients with diaphragmatic hernia is true referred pain.

The Treatment

The treatment of the patient with esophageal hiatus hernia when the lesion is small is essentially medical. Phrenicectomy or surgical repair is justified only in the large hernias or when medical measures fail to give relief from pain or bleeding.

The medical treatment consists of the following:

1) Diet. A smooth bland diet with frequent small feedings is essential. Rough and coarse vegetables are to be avoided. Gas forming vegetables like cabbage and sauerkraut are not desirable.
2) Medications.
   A) Atrophine sulphate and Tr. Belladonna are particularly indicated in the control of angina associated with gastrointestinal symptoms.
   B) Antacids like the aluminum hydroxide compounds are useful in combination with magnesium trisilicate.
   C) Nitroglycerine may relieve the acute symptoms of the hernia if it is taken before the intake of food or before retiring.
3) General Measures.
   A) Avoidance of alcohol and tobacco is important.
   B) Assumption of the upright position after eating is helpful.
   C) Avoidance of exercise immediately after a meal is urged.
   D) Avoidance of tight lacing or abdominal belts.
   E) Adequate mental and physical rest and sedation if and when indicated.
   F) Reduction in weight in the obese.

SUMMARY

1) Esophageal hiatus hernia is the most frequent type of diaphragmatic hernia.

2) Fluoroscopy and roentgenographic studies are essential for the diagnosis.

3) The hernia may be symptomless, but in my experience symptoms are frequently present.

4) Symptoms may be related to (a) gastrointestinal disturbance, (b) acute blood loss, (c) chronic blood loss or (d) angina pectoris type of pain suggestive of cardiac disease.

5) The treatment is generally medical consisting of diet, medication and general measures.

RESUMEN

1) La hernia del hiato esofágico es el tipo más frecuente de las hernias diafragmáticas.

2) Los estudios roentgenoscópicos y roentgenográficos son esenciales para hacer el diagnóstico.

3) La hernia puede ser asintomática pero, en mi experiencia, los síntomas ocurren con frecuencia.

4) Los síntomas pueden estar relacionados a (a) disfunción gastrointestinal, (b) pérdida de sangre aguda, (c) pérdida de sangre crónica o (d) dolor de tipo de angina pectoris que sugiere cardiopatía.

5) Por lo general, el tratamiento es médico y consiste de dieta, medicación y medidas generales.

RESUME

1) La hernie de l'orifice oesophagien est le type le plus fréquent de la hernie diaphragmatique.

2) La radioscopie et la radiographie sont les éléments essentiels sur lesquels se fonde le diagnostic.

3) Les hernies peuvent être parfaitement silencieuses, mais dans les cas qu'il à examinés, l'auteur à constaté la fréquence de manifestations symptomatiques.

4) Celles-ci peuvent être: (a) des troubles gastro-intestinaux, (b) une hémorragie aiguë, (c) des hémorragies chroniques, (d) une douleur rappelant l'angine de poitrine et faisant penser è une affection cardiaque.

5) Le traitement est habituellement médical et consiste en régime spécial, médications et mesures d'ordre général.

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The Cricothyroid Route for Anesthesia in Bronchoscopy*

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Anesthetic agents and anesthetic technics are always of interest to bronchologists, for good technic in bronchoscopy requires perfect anesthesia. Many years ago reports began to appear from Europe on a method that instilled the anesthetic agent directly into the larynx by way of a needle inserted through the cricothyroid ligament. This method became very popular in England and France for anesthetizing the tracheobronchial tree for bronchography.[1] It became familiar to many Americans stationed in England during the last World War. Although familiar to most bronchologists, many have been reluctant to employ it because of its theoretical dangers. Some, without trial, have doubted its effectiveness. For that reason we have utilized the cricothyroid route in 350 consecutive bronchoscopies to determine the value and limitations of this method. This is a report of our experience.

Before discussing the advantages and disadvantages of the cricothyroid route, it is necessary to view briefly the advantages and disadvantages of other technics of anesthesia for bronchoscopy, to give us a background against which our experiences can be evaluated. There are at present two popular methods of inducing anesthesia of the tracheobronchial tree. In the older and more widely used procedure, the anesthetic agent is dropped on the vocal cords under the guidance of a laryngeal mirror.[2] While this method is safe, the danger lies in the anesthetic agent. In trained hands this procedure is effective, but the casual operator will often induce imperfect anesthesia. Moreover, this technic is time-consuming, requiring about 20 minutes, and in busy clinics one individual must induce anesthesia while others perform the operative procedures. The method is difficult to employ in bed patients, and in sick or uncooperative individuals.

The second method is more recent in origin and consists of inhaling a microspray of an anesthetic agent.[3,4] This method demands less skill than the first, and therefore appears easier to perform. However, it too, is time-consuming, and in our experience does not always induce perfect anesthesia. Moreover, it requires good patient cooperation.

The technic which we have employed is as follows: The patient is placed in the supine position on the operating table. The pharynx is then sprayed with a 5 per cent solution of cocaine, using two or three squeezes of the handbulb. (The C. L. Jackson atomizer is excellent for this purpose as it

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frees one hand for retraction of the tongue.) After the pharynx has been sprayed, the neck is hyperextended. The neck is then sponged with a 70 per cent solution of alcohol and the space between the lower border of the thyroid cartilage and the upper border of the cricoid cartilage is palpated. A 20-gauge needle, with syringe attached, is then quickly thrust into the subcutaneous tissues in the midline of the neck, at the point selected by the palpating finger. A small amount of a 1 per cent solution of procaine is then instilled. The first thrust of the needle is made parallel to the plane of the table. The needle is then rotated to point perpendicular to the cricothyroid ligament and is quickly thrust through the ligament into the lumen of the larynx. Aspiration is performed at this point, and if large bubbles of air are not obtained, the needle is moved. No procaine solution is instilled into the trachea, as it induces violent coughing which may dislodge the needle. After the position of the needle has been confirmed by aspirating air, the syringe is quickly detached, and another syringe, previously loaded with 5 cc. of a 5 per cent solution of cocaine is attached. Aspiration is repeated, and if large bubbles of air are obtained, the cocaine solution is quickly injected and the needle is immediately withdrawn. This induces a violent fit of coughing which sprays the anesthetic solution over the larynx and bronchial tree. An alcohol sponge is promptly placed over the puncture site and this area is massaged. While doing this, the patient may sit up to cough. Five minutes should then elapse before beginning the bronchoscopy.

There are several points in our technic that require further discussion. Luer-Loc syringes are not used as they cannot be detached quickly, and speed is essential when changing syringes. The two-syringe method is employed because the cocaine solution is difficult to sterilize, and with the technic described, no unsterile solution can present itself at the needle point until the lumen of the larynx is reached. This helps prevent neck infections. We selected the 20-gauge needle after trying needles of various sizes. Smaller lumina do not permit rapid injection, and the patients become uncomfortable and try to cough and sit up before instillation is completed. Larger bore needles leave larger holes through which secretions may be coughed into the fascial planes of the neck. Spread through the puncture wound may also be prevented by massaging the puncture site. Another safety rule is to inject no solution if air does not bubble easily into the syringe.

There are several advantages to this "needle" method of anesthesia. Anesthesia is always satisfactory; it is always possible to introduce the bronchoscope through the larynx into the trachea without cough or laryngeal spasm making introduction difficult. The procedure is quickly performed, taking on the average two minutes. The method is simple and therefore can be used on patients unable or unwilling to sit up. It has been successfully employed on uncooperative patients. The technic is easily learned. After watching the procedure only a few times, residents have induced excellent anesthesia. There has been no difficulty with this technic in those patients who have had previous laryngeal surgery.

An unexpected objection to the cricothyroid method of anesthesia appeared in this study. In an occasional patient the post-instillation cough raises a slightly blood-tinged sputum. For that reason there may be some contraindication to the "needle" technic in patients undergoing examination for idiopathic hemoptysis. In our own experience, blood found on bronchoscopic examination has always been easily distinguished from traumatic bleeding. However, we have examined only 15 cases of idiopathic hemoptysis and our experience is therefore too limited to definitely settle this point.

We have also noted that 5 per cent of our patients require supplementary doses of the anesthetic agent when we are working in the far reaches of the bronchial tree. However, this happens with all methods of anesthesia, because thick secretions in those areas prevent good contact between the anesthetic agent and the bronchial mucosa.

Several people who have watched our clinics have expressed concern over the possibility of infections of the neck or fascial planes occurring if infected secretions should be coughed out along the needle tract. Our study was originally undertaken to determine if these theoretical objections were valid. In our series of 350 patients, we have had no infections of the neck or needle tract, although most of our bronchoscopies were done for patients with bronchiectasis, tuberculosis, lung abscess and pneumonias. We have, of course, observed the usual aseptic precautions. Harkin,[5] who employed a similar technic of anesthesia in 1,000 bronchoscopies, had but three cases of superficial neck infection. However, in his technic, he routinely punctured the cricothyroid ligament twice with an 18-gauge needle. We have found no need for two instillations of the anesthetic solution and our one puncture technic with a smaller gauge needle has resulted in no neck infections. We have bronchoscoped several individuals for four consecutive days and have observed no neck infections due to the repeated punctures and have noted no traumatic changes in the tracheal mucosa.

To avoid introducing too many variables into this study, we have employed but one anesthetic agent, a 5 per cent solution of cocaine in 5 cc. amounts. There have been no noteworthy reactions to this dose. Two patients felt a little uncomfortable after anesthesia was induced, and they may have had a slight cocaine reaction. One of the factors contributing to the almost total lack of reactions is the expulsion of from one to two cubic centimeters of the cocaine solution by the violent coughing that follows its instillation. Some credit may also be due to the preoperative use of nembutal, morphine and scopolamine.

SUMMARY

The cricothyroid technic of anesthesia is effective and safe for bronchoscopy. Its ease of induction also commends it.

RESUMEN

La técnica cricotiroidea de anestesia es eficaz e innocua para la broncoscopia. También recomiéndala la facilidad con que produce la anestesia.

RESUME

La technique cricothyroidienne d'anesthésie est effective et sans danger. La facilité avec laquelle on peut la réaliser est également une des raisons de l'utiliser.

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Temporary Plombage with Lucite Balls in Thoracoplasty

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From the end of 1949 to July, 1950, we used lucite balls (methyl methacrylate) as plombage in 52 patients on whom thoracoplasty was performed for pulmonary tuberculosis. In this report are presented the results of this experiment.

Our main purpose in filling the parietal pocket created by rib resection at the first stage thoracoplasty was to maintain the collapse already established and thus prevent any re-expansion of the lung until the next stage. In addition, we wished to avoid adhesions between the scapular and the intercostal muscles, thus making the second operation easier and also keeping the intercostal muscles approximated to the collapsed lung.

The results were as desired. The pocket created by the resected ribs is filled with lucite balls, and most of the retraction takes place as soon as the first stage is performed. It should be emphasized that this effect is not due to brutal pressure. Only a sufficient number of balls is used to fill the parietal space without harmful compression. The plombage keeps the lung collapsed, prevents its re-expansion, and even facilitates its progressive retraction. While postoperative fluoroscopy at first shows the apex to be still convex, a few days later it appears concave.

The second stage is made easier by the plombage. After the chest wall muscles are divided, the balls can be easily removed if the patient is re-operated after the usual interval or even two or three months later. The balls become encased in an elastic membrane and frequently a small amount of sero-fibrinous fluid or even fibrinous deposits are present. After the balls are removed, the upper part of the chest is a single free space, and there are no adhesions between the deep and superficial muscles layers. Consequently, the resection of additional ribs and antero-lateral stumps is more easily accomplished.

In most patients, a five or six rib thoracoplasty was performed in two stages. Plombage was inserted during the first stage and removed at the second stage. Experience showed that the plombage not only produced a better immediate collapse, but also a better final collapse. After this type of operation, the lung re-expands very little, and the parietal hydro-aeric pocket gradually disappears. This disappearance is due more to the depression of the anterior wall of the pocket than to re-expansion of the lung. In most patients, the final collapse was very satisfactory in the part of the lung corresponding to the resected ribs, as though the plombage inserted at the first stage had brought the apex down to a low position and fixed it there. Between the two stages the severed intercostal muscles become fibrous and the periosteum produces new bone. However, we do not believe that these two reasons are enough to explain the permanence

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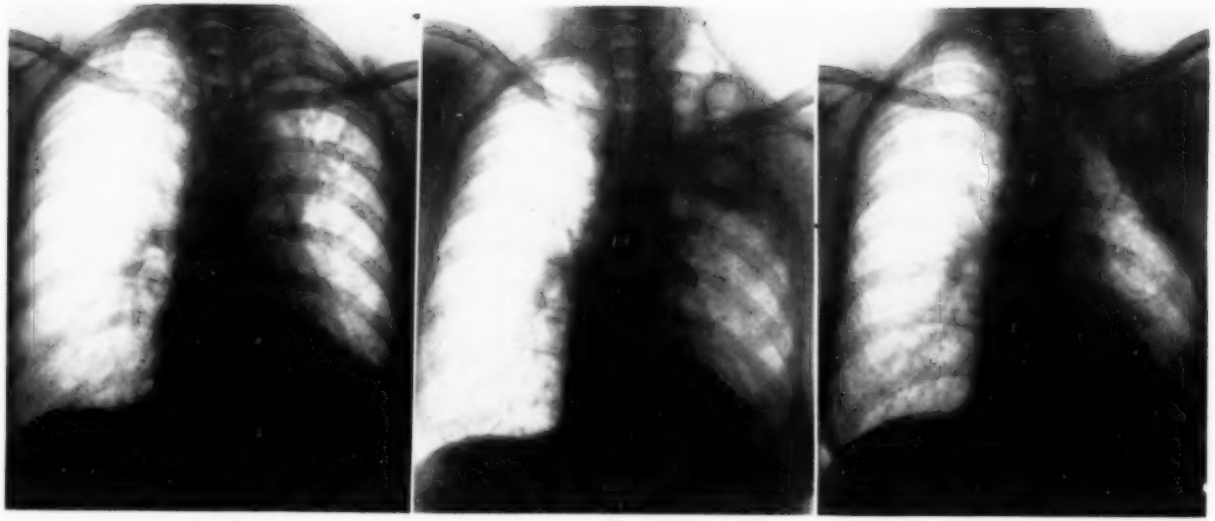

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1: Mme **A**. Pulmonary and bronchial disease in the upper third of the left lung. — *Figure 2:* Same patient. After first stage of thoracoplasty-resection of four ribs and plombage with seven balls. — *Figure 3:* Same patient. Four months after the second stage; reossifications have developed.

of the collapse. After thoracoplasties without plombage, the presence of blood-clots or serosanguinous fluid in the free space has not prevented re-expansion of the upper part of the lung in the months following operation. Therefore, we think that another factor must intervene and that the membrane, stimulated by plombage, must fix the collapse. For this reason, in patients recently operated, the outer wall of the pocket was mobilized and fastened to the inner one in order to maintain a better collapse.

In some patients who needed a three stage sub-total thoracoplasty because of tuberculous lesions involving a large area of lung, lucite balls were inserted again at the second stage.

In other cases, we performed upper thoracoplasties in which plombage was not removed at the last stage. These operations have been performed on patients who had very destructive lesions or irretractile cavities in the upper third or half of the lung. In this situation, one stage was performed, resecting only four ribs or more often there were two stages and the plombage was replaced at the second stage. This technique gives the maximum pulmonary retraction. With a five or six rib thoracoplasty, it permits the inferior angle of the scapula to rest on the ribs, thus causing no obvious deformity of the chest. The functional value of the lower lobe is preserved, and a radiologic amputation of the upper lobe is obtained. It apposes the walls of irretractile cavities and may allow them to heal.

It is our opinion that these permanent plombages are not dangerous because they are separated from pulmonary lesions by intercostal muscle and periosteum. Lucite balls can only migrate outwards, i.e. into the axilla, and this is not dangerous. Nevertheless, in most of our patients, plombage was removed four to eight months after the last stage of thoracoplasty, since it becomes useless after reossification is well enough developed to be seen by x-ray inspection. As a rule, we think it much better not to allow a foreign body to remain in the tissues, even though it may be well tolerated.

Our knowledge of thoracoplasty with lucite ball plombage is still too limited to allow valuable statistical results to be given. However, without any doubt, its effect on pulmonary lesions is more rapid and more constant

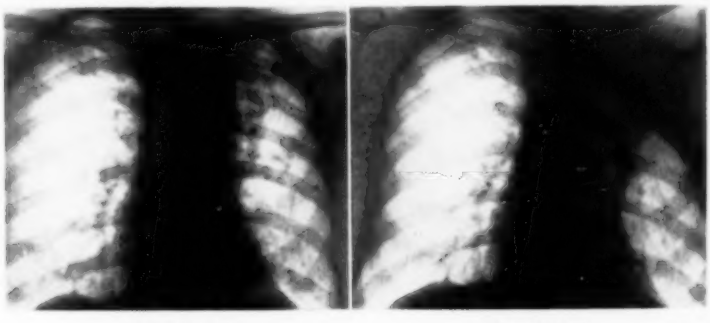

FIGURE 4 FIGURE 5

Figure 4: Mr. L. Left infraclavicular cavity in a patient 50 years old — *Figure 5:* Same patient. Two months after the second stage of a five-rib thoracoplasty.

than that obtained with any other type of thoracoplasty. On the other hand, the use of such a plombage restricts the number of ribs that must be resected. Thus, it reduces the functional impairment due to thoracoplasty and preserves the function of the non-collapsed pulmonary tissue. It also avoids the deformities due to poor position of the scapula.

In our experience, the use of plombage under these conditions does not increase the operative risk. In this series of 52 cases subjected to thoracoplasty, no infection was noted and no migration of the balls towards the mediastinum or lung occurred. Some balls migrated under the skin of the axilla when the plombage remained in place for several months, but this proved harmless. No spread to the homolateral base or opposite lung was observed.

During the years prior to this experiment, the results of thoracoplasty without plombage had led us to extend the indications for extrapleural pneumothorax. The ratio of extrapleural pneumonolysis to thoracoplasty was two to one. As it is performed in France, extrapleural pneumothorax gives satisfactory results and few complications. From the point of view of respiratory function it is excellent. But we think that this type of operation should be reserved for patients who have recent lesions susceptible to sound cicatrization under the action of temporary air collapse and in addition who are under 45 when extrapleural pneumonolysis is very easy.

The results observed in thoracoplasty with lucite ball plombage led us to modify our indications. Now more thoracoplasties than extrapleural pneumonolyses are performed because the results are equally good with upper thoracoplasties limited to five or six ribs, and because permanent collapse seems to give greater security for the future than temporary air collapse.

SUMMARY

Of 52 patients on whom thoracoplasty was performed, plombage with lucite balls was put in place between the operative stages. This technique

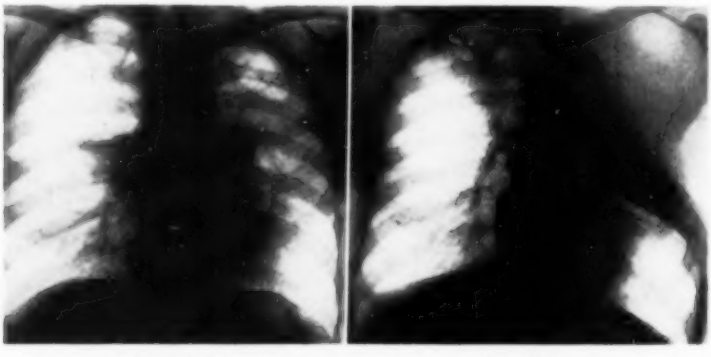

FIGURE 6 FIGURE 7

Figure 6: Mr. D. Big cavity in the left apex. Right artificial pneumothorax.—*Figure 7:* Same patient. Six months after second stage of a six-rib thoracoplasty and reexpansion of the right lung.

increases the extent of the collapse and makes the secondary operations easier. In some patients with ulcerative and irretractile lesions of the upper part of the lung, a plombage was reinserted at the second stage; the collapse thus realized is much improved and joins the walls of irretractile cavities.

This experiment shows that the plombage improves the results of thoracoplasty, and it restricts the number of ribs resected. Thus, it reduces the functional and anatomical mutilation due to the operation. On the other hand, the plombage is not in close contact with the lung and mediastinum; it does not appreciably increase the risks of thoracoplasty.

RESUMEN

En 52 pacientes, en quienes se practicó toracoplastía, se aplicó plombaje con esferas de Lucita, entre los tiempos operatorios. Esta técnica hace aumentar la extensión del colapso, y facilita las operaciones subsecuentes.

En algunos pacientes con lesiones ulcerosas y no retráctiles de la parte superior del pulmón, se reinsertó un plombaje en el segundo tiempo; el colapso así realizado mejora mucho y reúne las paredes de las cavidades no retráctiles.

Esta experiencia demuestra que el plombaje mejora los resultados de la toracoplastía, y restringe el número de costillas resecadas. De este modo se reduce la mutilación funcional y anatómica causada por la operación. Por otra parte, el plombaje no está en contacto directo con el pulmón y el mediastino; no hace aumentar apreciablemente los riesgos de la toracoplastía.

RESUME

Chez 52 malades pour lesquels fut réalisée une thoracoplastie, l'auteur a pratiqué le plombage par billes de lucite, mises en place entre les temps opératoires. Cette technique augmente l'importance du collapsus et rend plus facile le second temps opératoire. Chez certains malades atteints de lésions ulcératives et irrétractiles, de la partie supérieure du poumon, le plombage fut introduit de nouveau lors du second temps; le collapsus ainsi réalisé est beaucoup plus efficace et réussit à amener la fermeture des cavités irrétractiles.

Cet essai montre que le plombage améliore les résultats de la thoracoplastie et diminue le nombre de résections costales nécessaires. De la sorte, il réduit également les troubles fonctionnels et anatomiques consécutifs à l'intervention. Par ailleurs, le plombage n'est pas en contact intime avec le poumon et le médiastin; il n'augmente pas de façon appréciable les dangers de la thoracoplastie.

The Effect of Chronic Pulmonary Suppuration on the Gastric Mucosa*

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The ingestion of purulent material from such conditions as chronic gingivitis, sinusitis, bronchitis, bronchiectasis, and lung abscess has frequently been suggested as one cause of the inflammatory reaction of the gastric mucosa found in chronic gastritis. For this reason, a group of 17 patients with chronic pulmonary suppurative disease was examined gastroscopically in order to detect the presence of any abnormalities of the gastric mucosa.

The group consisted of 15 men (aged 18 to 67 years, average 31.4 years) and two women (aged 32 and 60) having either bronchiectasis or lung abscess with production of purulent sputum (Table I). The diagnosis was established in all cases by the usual methods—radiography and bronchography with lipiodol. Sputum cultures were obtained in only five cases, but microscopic examination of the sputum ruled out tuberculosis in every case.

Prior to gastroscopy the esophagus and cardia were examined by fluoroscopy to rule out any contraindications to the procedure, viz., esophageal diverticula or obstruction at the cardia. If gastric secretions were present at the time of gastroscopy, stained smears were made of the aspirate. The gastroscopic examination was carried out under local anesthesia with the patient lying on the left side.

Gastroscopy revealed an entirely normal mucosa in all but two instances: 1) mucosal edema of the gastric antrum (Cases 2 and 6) localized atrophic gastritis (Case 16). Only two of the patients had mild gastrointestinal complaints; two others had intermittent anorexia which probably could be ascribed to the primary pulmonary disease. The gastric mucosa of these four patients, however, was normal.

Stained smears of the gastric secretion from six of the patients demonstrated many polymorphonuclear leukocytes, a few columnar and squamous epithelial cells, probably of respiratory tract origin, and much debris. Subsequent autopsy in one instance (Case 14) disclosed no abnormalities of the stomach.

Discussion

Three types of gastritis may be identified by gastroscopic examination. Superficial gastritis is associated with reddened, engorged mucosal folds to which much mucous is adherent. Small erosions may be present. The atrophic type displays fine, branching red or blue submucosal vessels, ren-

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The opinions expressed are those of the authors, and do not necessarily reflect the views of the Medical Department of the Navy or of the Navy Department.

TABLE I: SUMMARY OF CASES

Case No.	Sex	Age	Pulmonary Disease	Daily Amount and Duration of Sputum Production	Gastroscopic Findings
1.	M	18	Left lower lobe bronchiectasis with pneumonitis.	1 to 3 oz. dark gray sputum; 10 months.	Normal.
2.	M	19	Bilateral lower lobe bronchiectasis.	1 to 2 oz. foul sputum; "since childhood"	Normal—much purulent debris.
3.	M	19	Left lower lobe bronchiectasis.	4 to 8 oz. yellow sputum; 2 years.	Normal.
4.	M	19	Bilateral lower lobe bronchiectasis.	½ oz. yellow sputum; "since childhood"	Normal.
5.	M	22	Bilateral lower lobe bronchiectasis with pneumonitis.	3 oz. gray-green sputum; 3½ years.	Normal—much purulent debris.
6.	M	22	Right lower lobe bronchiectasis.	2 oz. yellow sputum; 3 years.	Edema of antrum.
7.	M	23	Bilateral lower lobe bronchiectasis.	3 to 6 oz. yellow, foul sputum; 2½ years.	Normal.
8.	M	28	Bilateral lower lobe bronchiectasis.	½ oz. yellow sputum; 3 years.	Normal.
9.	M	30	Bronchiectasis.	4 oz. yellow sputum; 9 months.	Normal.
10.	M	31	Bilateral lower lobe bronchiectasis.	3 to 6 oz. yellow, foul sputum; 2½ years.	Normal.
11.	F	32	Left upper and left lower lobe bronchiectasis.	1 to 6 oz. gray, foul sputum; 10 years.	Normal.
12.	M	36	Bilateral lower lobe bronchiectasis.	2 oz. yellow sputum; 2 years.	Normal.
13.	M	43	Lung abscess.	4 oz. yellow sputum; 1 month.	Normal.
14.	M	46	Right lower lobe bronchiectasis.	4 to 8 oz. yellow sputum; 8 months.	Normal.
15.	M	49	Bronchiectasis.	3 oz. foul, yellow sputum; 20 years.	Normal.
16.	F	60	Bronchiectasis.	2 oz. foul, yellow sputum; 18 years.	Localized atrophy, anterior wall.
17.	M	67	Left lower lobe bronchiectasis.	4 to 8 oz. yellow sputum; 3 months.	Normal.

dered visible by the atrophy of the overlying, thinned, translucent mucosa. Hypertrophic gastritis presents a dull, velvety appearance of the mucosa, the folds of which, if not engorged, at least appear rigid and cobblestoned.

The gastric mucosal abnormalities noted in two patients in this group were not considered significant. Mucosal edema is often a transient phenomenon and in no way implies organic change. The localized gastritis in one patient was not considered to be the result of the prolonged swallowing of purulent material since the mucosal changes were limited in extent and could readily be related to the fact that this patient was 60 years old.

Bockus[1] has stated that the prolonged swallowing of mucopurulent material may create chronic gastritis if achlorhydria is present. The investigations of Dick[2] demonstrated the presence of myriads of bacteria, including E. coli, in the gastric juice of patients with pernicious anemia. In simple achlorhydria, cultures of gastric juice presented the same flora as the saliva. Since gastritis is not necessarily associated with either achlorhydria or pernicious anemia,[3] the mere presence of viable bacteria would not appear to be of significance in the genesis of gastritis.

Hardt[4] reported an incidence of atrophic gastritis in 52.8 per cent of patients with advanced pulmonary tuberculosis complicated by intestinal tuberculosis. Other factors than the swallowing of pathogenic bacteria, however, were no doubt present.

SUMMARY

Gastroscopic examination of 17 patients with bronchiectasis or lung abscess revealed a fully normal mucosa in all but two instances, both of which were of minor importance. The ingestion of lesser amounts of purulent material due to purulent gingivitis or chronic sinusitis, therefore, would not appear to be harmful to the gastric mucosa.

RESUMEN

El exámen gastroscópico de 17 enfermos con bronquiéctasis o absceso pulmonar reveló un mucosa normal en todos menos dos de ellos pero estos dos casos eran de importancia menor. La ingestión de menores cantidades de material purulento debido a gingivitis purulenta o a sinusitis crónica, por tanto, no parece dañar la mucosa gástrica.

RESUME

L'examen gastroscopique de 17 malades atteints de bilatation des bronches ou d'abcès du poumon a montré une muqueuse parfaitement normale, sauf dans deux cas qui étaient d'un intérêt médiocre. En conséquence, l'ingestion de quantités moindres de pus, comme cela peut exister dans la gingivite purulente ou les sinusites chroniques ne pourrait être considérée comme pouvant créer un dommage à la muqueuse gastrique.

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Phrenic Paralysis Following Cervical Rib Resection*

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This report deals with two cases of accidental temporary phrenic paralysis secondary to surgical procedures in the neck for the scalenus anticus syndrome. The first had a right anterior scalenotomy and partial resection of a cervical rib, while the second had a left anterior scalenotomy. A review of the Quarterly Cumulative Index for the past ten years reveals no previously reported case of this nature.

The first case with bilateral cervical ribs had evidence of brachial plexus irritation on the right side. The right scalenus anticus was severed at operation and the cervical rib was partially resected; it is believed the associated phrenic nerve was cut across since no mention of it was made in the surgical report. Complete paralysis persisted for one year; normal motion had returned at the end of 15 months. The second case had bilateral cervical ribs but had symptoms of a scalenus anticus syndrome on the left. The left scalenus anticus was severed at operation after the phrenic

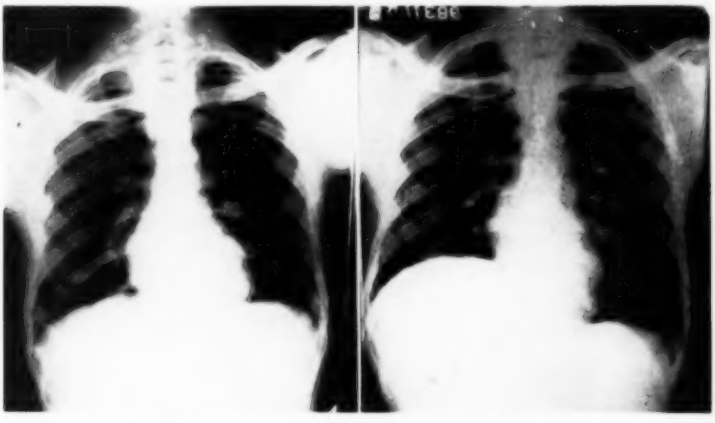


FIGURE 1 FIGURE 2

Figure 1: The preoperative x-ray film: A cervical rib can be seen on the right side and minimum widening of the right superior mediastinum. Both leaves of diaphragm are in their normal positions.—*Figure 2:* Chest x-ray film made after resection of the cervical rib: There is marked elevation of right leaf of the diaphragm. Upon fluoroscopy the movement was paradoxical. The previously noted cervical rib was no longer visualized.

*From the Tuberculosis Service, Veterans Administration Center, Dayton, Ohio, and the College of Medicine, University of Cincinnati.

†Chief, Tuberculosis Service; Instructor of Medicine.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

nerve had been isolated. It is felt that during the process of retraction of the nerve a traumatic neuritis had resulted causing the subsequent diaphragmatic paralysis. Complete paralysis persisted for six months, with gradual return of function thereafter.

The phrenic nerve bears an intimate relationship to the scalenus anticus muscle[1] but despite this fact, no previous reports have been published of phrenic paralysis following surgery for the scalenus anticus syndrome or following removal of a cervical rib.

A careful analysis of the preoperative and postoperative films, even in the absence of a history, might lead to the correct diagnosis. In the first case the development of an elevation of a previously normally placed diaphragm, associated with the absence of a portion of the right cervical rib might well lead one to a correct reconstruction of the intervening events. In the second case the cervical rib was not removed, but the appearance of a phrenic paralysis in a patient who has a cervical rib on the same side should be thought of as possibly representing the result of surgery for the scalenus anticus syndrome.

SUMMARY

1) Two patients who have had surgery for the scalenus anticus syndrome developed phrenic paralysis subsequent to and apparently as a result of the scalenus anticus operation.

2) This was due, in all probability, to trauma to the phrenic nerve in each case.

3) This condition has apparently not been previously reported.

RESUMEN

1) Dos enfermos a quienes se operó por el síndrome del escaleno anterior presentaron parálisis del nervio frénico y aparentemente como resultado de la operación del escaleno anterior.

2) Con toda probabilidad esto se debió a trauma del frénico durante la operación en los dos casos.

3) Aparentemente esto no había sido referido antes.

RESUME

1) Deux malades qui avaient subi une résection de la première côte furent atteints de paralysie phrénique à la suite de l'intervention.

2) Selon toute probabilité, la cause en est le traumatisme du nerf phrénique.

3) Il ne semble pas que jusqu'à présent de tels cas aient été rapportés.

REFERENCE

Cunningham: "Text Book of Anatomy," 5th Ed. 1926, Wm. Wood & Co., New York.

19th Annual Meeting
American College of Chest Physicians

The preliminary scientific program for the 19th Annual Meeting of the College, to be held at the Hotel New Yorker, New York City, May 28 through 31, 1953, was published in the February issue of *Diseases of the Chest*. It is planned to publish the final program in the April issue of the journal.

Dr. Arthur M. Olsen, Chairman of the Committee on Scientific Program, and the members of his committee have organized an excellent group of subjects for discussion. More emphasis is being given to panel discussions, which will permit greater audience participation.

The round table luncheon meetings, which are in great demand at every annual session and are usually sold out in advance, will be repeated this year with many new topics and discussors.

New York City is celebrating its 300th Anniversary this year and the New York State Chapter of the College has arranged an excellent social program for the College meeting to commemorate this occasion.

LAST CALL FOR MANUSCRIPTS
1953 COLLEGE ESSAY AWARD

The Board of Regents of the American College of Chest Physicians offers a cash prize award of two hundred fifty dollars ($250.00) to be given annually for the best original contribution, preferably by a young investigator, on any phase relating to chest disease.

The prize is open to contestants of other countries as well as those residing in the United States. The winning contribution will be selected by a board of impartial judges and the award, together with a certificate of merit, will be made at the forthcoming annual meeting of the College, to be held in New York City, May 28-31, 1953. Second and Third prize certificates will also be awarded.

All manuscripts submitted become the property of the American College of Chest Physicians and will be referred to the Editorial Board of the College journal, *Diseases of the Chest*, for consideration. The College reserves the right to invite the winner to present his contribution at the annual meeting. Contestants are advised to study the format of *Diseases of the Chest* as to length, form and arrangement of illustrations, to guide them in the preparation of the manuscript.

The following conditions must be observed:

(1) Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, not later than April 15, 1953.

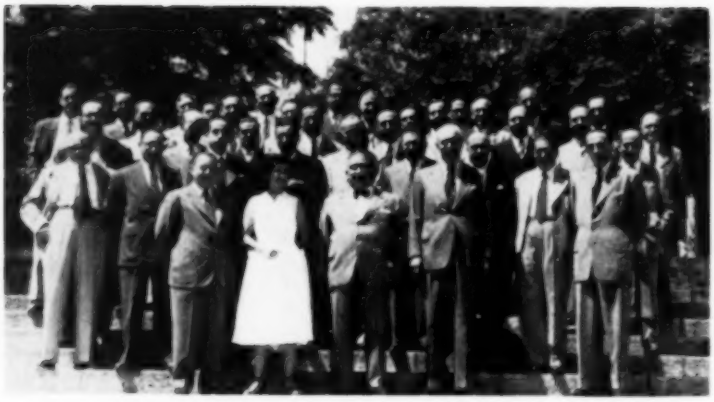
(2) The only means of identification of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

COLLEGE SEMINARS

A group of six seminars on timely subjects will be presented at the Hotel New Yorker, New York City, on Wednesday, May 27. The registration fee is $7.50 for each seminar which is comprised of a series of three lectures. Further information may be obtained by writing to the Executive Offices of the College in Chicago.

College Chapter News

ARGENTINE CHAPTER



The Seventh Annual Meeting of the Argentine Chapter of the American College of Chest Physicians was held in Alta Gracia on December 20, 1952, at which time officers for 1953 were elected: Dr. Rodolfo Cucchiani Acevedo, Buenos Aires, President; Dr. Oscar Cames, Rosario, Vice-President; Dr. Jorge A. Doyle, San Fernando, Secretary-Treasurer.

Following the business meeting, a scientific program was presented on the theme "Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis and other Diseases of the Chest" discussed by Drs. Rodolfo Cucchiani Acevedo, Bruno Biondini, Mario A. Chaneton, Francisco Arambarri, Isaac F. Wolaj, Raul Ortiz, Carlos M. Quinteros, Carlos Walter Grobli, Jorge A. Doyle, Juan Carlos Rey, Pedro Rubinstein, Hector Fratti, and Alberto Soubrie.

ILLINOIS CHAPTER

The Illinois Chapter held a dinner meeting and scientific session at the St. Clair Hotel, Chicago, February 20, 1953. The scientific program was presented by faculty members of the University of Chicago.

CALIFORNIA CHAPTER

The Northern California section of the California Chapter met at the Bellevue Hotel, San Francisco, January 24, 1953. Speakers at this meeting were: Dr. Andrew L. Banyai, Milwaukee, Wisconsin, President of the College, Dr. Alvis E. Greer, Houston, Texas, President-Elect of the College, and Dr. Edgar Mayer, New York, New York, Regent for New York state.

MISSOURI CHAPTER

The Missouri Chapter will hold its annual meeting at the Hotel President, Kansas City, Missouri, April 26, in conjunction with the Missouri Trudeau Society. Dr. David B. Radner, Chicago, Illinois, Assistant Professor of Medicine, Chicago Medical School and Director, Chest Department, Michael Reese Hospital will be guest speaker. His topic is "Prevention of Postoperative Broncho-pulmonary Complications."

FLORIDA CHAPTER

The Florida State Chapter will meet April 26, 1953 in Hollywood, Florida. After a business session, the following program will be presented:

"The Management of the Asthmatic,"
Maurice Kovnat, Miami Beach.

"Hemoptysis of Undetermined Origin,"
Nathaniel M. Levin, Miami.

"The Treatment of Pulmonary Tuberculosis with Isonicotinic Acid Alone and Combined with other Antibiotics,"
Jack Reiss and George L. Baum, Coral Gables.

"INH in the Treatment of Pulmonary Tuberculosis,"
Antonio Perez and Henry C. Sweany, Tampa.

"Bronchial Adenoma,"
Ivan C. Schmidt, Lantana.

"Papillomatosis of the Bronchial Tree,"
Burnett Schaff and R. V. Thomson, Coral Gables.

"Concomitant Bronchogenic Carcinoma and Pulmonary Tuberculosis,"
Hawley H. Seiler, Tampa.

X-Ray Conference.

OKLAHOMA CHAPTER

Members of the College in the State of Oklahoma will hold their first meeting for formation of the Oklahoma Chapter, April 12, 1953, at the Mayo Hotel, Tulsa. After the business meeting and election of officers, the following program will be presented:

"Management of Pulmonary Emphysema,"
Robert M. Shepard, Jr., Tulsa.

"Surgery of Acquired Heart Disease,"
Robert R. Shaw, Dallas, Texas.

X-Ray Conference,
Moderator: Robert M. Shepard, Sr., Tulsa.

POTOMAC CHAPTER

The Potomac Chapter of the College will hold its annual meeting at the Greenbriar Hotel, White Sulphur Springs, West Virginia, on April 10. A morning and an afternoon scientific session will be presented, closing with an x-ray conference. There will be a luncheon meeting with Irvin Stewart, LL.B., Ph.D., LL.D., President of the University of West Virginia, as guest speaker. Dr. Stewart will talk on "The New Medical Education Program for West Virginia."

The program to be presented is as follows:

President's Address: George R. Maxwell, Morgantown, West Virginia,
President, Potomac Chapter,
"Rene Theophile Hyacinthe Laennec — 1781-1826."

"The Diagnosis and Surgical Treatment of Emphysema."
Otto C. Brantigan, Baltimore, Maryland.

"The Surgical Treatment of Mitral Stenosis."
Edgar W. Davis, Washington, D. C.

"Bronchial Adenoma,"
M. Lawrence White, Huntington, West Virginia.

"Expansion of the Lung of the New Born" (motion picture),
Vernon Krahl, Baltimore, Maryland.

"Diagnosis and Management of Chylothorax,"
Roy G. Klepser, Washington, D. C.

SOUTH AFRICAN CHAPTERS

Standing (left to right): A. Rabinowitz, D. I. Adler, J. O. Marais, L. A. Westwood, M. H. Goldberg, W. S. Linton, D. N. Fuller, B. A. Horwitz.—*Seated* (left to right): L. Fatti, H. O. Hofmeyr, M. A. Pringle, D. P. Marais, W. L. Phillips, G. R. Crawshaw, and M. Kuper.

The Southern and Northern Chapters of the Union of South Africa presented, for the first time, a Section on Diseases of the Chest, during the Annual South African Medical Congress which was held in Johannesburg from September 21st through the 27th, 1952.

Dr. David P. Marais, Regent of the American College of Chest Physicians for South Africa, presided over the Chest Section, with Dr. Maurice Pringle, Governor of the College for the Northern States, as Secretary.

WEST BENGAL CHAPTER

The West Bengal (India) Chapter elected Dr. A. C. Ukil, Calcutta, President; Dr. N. N. Sen, Calcutta, was elected Vice-President, and Dr. P. K. Ghosh, Calcutta, was elected Secretary-treasurer at their meeting held in Calcutta, January 19, 1953.

TEXAS CHAPTER

The Texas Chapter will meet jointly with the Texas State Medical Society, Houston, Texas, April 26-29, 1953.

COURSE IN BRONCHOESOPHAGOLOGY

The University of Illinois College of Medicine will present a course on Bronchoesophagology, March 16-28, 1953, under the direction of Dr. Paul H. Holinger.

For information please write directly to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk St., Chicago 12, Illinois.

PAN PACIFIC TUBERCULOSIS CONFERENCE

A Pan Pacific Tuberculosis Conference under the joint sponsorship of the Department of Health, Republic of the Philippines, the World Health Organization, and the Philippine Tuberculosis Society will be held in Manila April 13-19, 1953. The opening session will be at the auditorium of the Far Eastern University and the scientific session will be at the Quezon Institute Conference Hall. Inquiries on attendance and participation to and about the conference may be addressed to The Secretariat: 1739 Rizal Avenue or P. O. Box 2049, Manila, Philippines.

College News Notes

Dr. Otto L. Bettag, Chicago, former Medical Director and Superintendent of the Chicago Municipal Tuberculosis Sanitarium, was recently appointed Director of Public Welfare of the State of Illinois by Governor William G. Stratton.

Dr. Benjamin Gasul, Chicago, has recently been appointed Clinical Associate Professor at the University of Illinois College of Medicine.

Dr. Arden Freer, Washington, D. C., former Governor of the College for the Veterans Administration, recently retired as Deputy Chief Medical Director of the Veterans Administration and has accepted an appointment to serve as special advisor to the Chief Medical Director on a consultatory basis. Dr. Roy A. Wolford, Washington, D. C. has succeeded Dr. Freer as Deputy Chief Medical Director and has also been appointed Governor of the College for the Veterans Administration.

Dr. Meyer R. Lichtenstein, Dr. George C. Turner, and Dr. William M. Lees, Chicago, participated in a program on Isoniazid Therapy presented before the Chicago Tuberculosis Society at the St. Clair Hotel, Chicago, January 30, 1953.

Dr. Hugh L. Houston, Murray, Kentucky, and Dr. Earl R. Gernert, Louisville, Kentucky, have been appointed members of the Council for the Control of Tuberculosis of the Kentucky State Medical Society.

Dr. Karl Pfuetze, Chicago, spoke before the Knox County Medical Society, Galesburg, Illinois, on "Antibiotics in the Treatment of Tuberculosis," January 15, 1953. Dr. Pfuetze is Chairman of the College Committee on Chemotherapy and Antibiotics.

Dr. Anthony J. Lanza, New York City, and Dr. Otto L. Bettag, Chicago, were discussants on the subject "A Community Looks at Industrial Health" at the Thirteenth Annual Congress on Industrial Health, at the Drake Hotel, Chicago, January 21, 1953.

Dr. David B. Radner, Chicago, spoke on "The Newer Antimicrobial Treatment in Tuberculosis" before Medical Unit 9-20, U. S. Naval Reserve, January 27, 1953.

The Annual Meeting of the Medical Society Executives Conference will be held at the Belmont Plaza Hotel, New York City, June 1, 1953. Mr. Murray Kornfeld, Executive Director of the American College of Chest Physicians, has been invited to organize the program for the conference of National Medical Societies.

Dr. Charles A. Smolt, Ventura, California, is planning a trip to France, Switzerland, Italy, and Greece in April and May. Dr. Smolt has been invited to present a lecture before the Italian Chapter of the College in Rome.

Dr. George G. Ornstein, New York City, spoke on "Isoniazides and Pulmonary Function" before the Palm Beach Medical Society, Palm Beach, Florida, February 23, and before the staff of the Veterans Administration Hospital, Coral Gables, Florida, February 27.

Brigadier General James P. Cooney, MC, Washington, D. C., has been appointed special assistant to the Commanding General, Walter Reed Army Medical Center, Washington, D. C. General Cooney was formerly Surgeon to the Japan Logistical Command.

Dr. Maurice S. Segal, Boston, Massachusetts, spoke before the Schenectady County Medical Society, Schenectady, New York, February 3, on "Chronic Emphysema and Its Management."

The December, 1952 issue of *Medical Record and Annals*, edited by Dr. Alvis E. Greer, Houston, Texas, President-Elect of the College, was dedicated to the American College of Chest Physicians. The following articles appearing in this issue were contributed by members of the College:

"Bronchogenic Carcinoma,"
Alton Ochsner, New Orleans, Louisiana.

"Postgraduate Education,"
Hollis E. Johnson, Nashville, Tennessee.

"Lung Cancer; An Appraisal of Its Changing Status,"
Seymour M. Farber, David A. Wood and Orville F. Grimes, San Francisco, California.

"Breathing Exercises and Allied Aids to Breathing in the Treatment of Pulmonary Emphysema,"
Alvan L. Barach, New York, New York.

"The Mechanism of Improvement in Apparently Permanent Pulmonary Disability,"
Edward R. Levine, Chicago, Illinois.

"The Tuberculin Reaction: Its Relative and Actual Importance,"
Jay Arthur Myers, Minneapolis, Minnesota.

"Cystic Disease of the Lungs: Report of Two Cases,"
Alvis E. Greer, Houston, Texas.

"Hypertrophic Emphysema: Its Pathogenesis, Pathomechanics and Modern Treatment,"
Andrew L. Banyai, Milwaukee, Wisconsin.

"Postwar Teaching of Tuberculosis,"
Charles M. Hendricks, El Paso, Texas.

Dr. George R. Maxwell of Morgantown, West Virginia, was Moderator of a Symposium on Coal Miner's Pneumoconiosis held on November 24. The program included papers by the following members of the College:

"Clinical Aspects of Coal Miner's Pneumoconiosis,"
Peter A. Theodos, Philadelphia, Pennsylvania.

"X-Ray and Gross Pathology,"
Louis L. Friedman, Birmingham, Alabama.

"Lung Biopsy,"
Louis Mark, Columbus, Ohio.

Dr. Eli H. Rubin of New York City was guest speaker and participated in clinics and conferences at the 26th Annual Refresher Course given by the Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, October 20-24, 1952.

ERRATUM

On page 120 of the January issue of *Diseases of the Chest*, Dr. Fernand Hebert was erroneously listed as appearing in the photograph of officials of the College being greeted at the Montreal airport upon arrival to attend the organizational meeting of the Quebec Chapter. The gentleman second from the left is Dr. Jean Louis Pilon, President of the Societe de Phtisiologie de Montreal.

AMERICAN HEART ASSOCIATION MEETING

The American Heart Association announces that the Twenty-Ninth Annual Meeting and the Twenty-Sixth Scientific Sessions will be held at the Hotel Chelsea in Atlantic City, New Jersey, April 8-12, 1953, immediately preceding the annual meeting of the American College of Physicians.

Committee on Motion Pictures

The following motion picture films have been approved by the Committee on Motion Pictures of the American College of Chest Physicians:

ANATOMY, PHYSIOLOGY AND EMBRYOLOGY

Cardiac Arrythmias (1949) (By Robert H. Shuler, Ph.D., M.D., Mark F. Hance, M.D., Richard Shaw, M.D. and David MacDougal, M.D., Chicago). 1½ reels; 16 mm.; silent and color. Procurable from Abbott Laboratories, North Chicago, Illinois.

The Heart Beat Mechanism in Health and Disease (1933) (By Clayton J. Lundy, M.D., Chicago). 11 reels; 16 mm.; silent. Procurable from American Heart Assn., 1775 Broadway, New York, New York.

Angina Pectoris, A Summary of Objective Studies (1942) (By Joseph E. F. Riseman, M.D., Boston). 6 reels; 16 mm.; sound and color. Procurable from Harvard Film Service, Inc., 421 Washington Street, Somerville, Massachusetts.

The Effects of Metallic Ions and Osmotic Disturbances on the Heart (1945) (By K. G. Wakim, M.D., Ph.D., Bloomington, Indiana). 1 reel; 16 mm.; sound. Procurable from Audio-Visual Center, Indiana University, Bloomington, Indiana.

Oxygen Therapy in Heart Disease (Produced in cooperation with the American Heart Association) (1946). 3 reels; 16 mm.; sound. Procurable from The Linde Air Products Company, 30 East 42nd Street, New York, New York.

Congenital Malformations of the Heart (Part I: Development of the Normal Heart). 600 ft.; 16 mm.; sound and color. Procurable from Instructional Materials Center, University of Washington, Seattle, Wash. (Sale $115; Loan $2.25).

Congenital Malformations of the Heart (Part II: Acyanotic Congenital Heart Disease). 600 ft.; 16 mm.; sound and color. Procurable from Instructional Materials Center, University of Washington, Seattle, Washington (Sale $115; Loan $2.25).

Congenital Malformations of the Heart (Part III: Cyanotic Congenital Heart Disease). 600 ft.; 16 mm.; sound and color. Procurable from Instructional Materials Center, University of Washington, Seattle, Washington (Sale $115; Loan $2.25).

Patent Ductus Arteriosus — Physiology, Diagnosis and Clinical Considerations (1952) (By George H. Humphreys II, M.D., New York, New York). 13 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $125; Rental $8.50).

Surgical Treatment for Congenital Pulmonary Valvular Stenosis (1950) (By George H. Humphreys II, M.D., New York, New York). 20 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $125; Rental $8.50).

Coarctation of the Aorta—Demonstration of Anatomy, Physiology and Surgical Treatment (1948) (By John C. Jones, M.D., Los Angeles, California). 2¼ reels; 16 mm.; sound and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

The Dynamics of Respiration (1944) (Medical School, University of Wisconsin, Dept. of Anesthesia, Radiology and Photography). 3 reels; 16 mm.; silent and color. Procurable from American Medical Association, Committee on Medical Motion Pictures, 535 North Dearborn Street, Chicago 10, Illinois.

ANESTHESIA

Intravenous Anesthesia and Tracheal Intubation (1950) (By Glenn Potter, M.D., Los Angeles, California). 45 mins.; 16 mm.; sound and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

Endotracheal Anesthesia (1944) (Prepared for use in training anesthetists in Great Britain; supervised by Dr. I. W. McGill and the anesthetics staff of Westminster Hospital, London). 2¼ reels; 16 mm.; sound. Procurable from International Film Bureau, 6 North Michigan Avenue, Chicago 2, Illinois.

Endotracheal Anesthesia (1949) (By Charles F. McCuskey, M.D., Los Angeles). 2 reels; 16 mm.; sound and color. Procurable from E. R. Squibb & Sons, 745 Fifth Avenue, New York 22, New York.

The Dynamics of Respiration (1944) (Medical School, University of Wisconsin, Department of Anesthesia, Radiology and Photography). 3 reels; 16 mm.; silent and color. Procurable from American Medical Association, Committee on Medical Motion Pictures, 535 North Dearborn Street, Chicago 10, Illinois.

CARDIOVASCULAR SYSTEM

Cardiac Arrythmias (1949) (By Robert H. Shuler, Ph.D., M.D., Mark F. Hance, M.D., Richard Shaw, M.D. and David MacDougal, M.D., Chicago, Illinois). 1½ reels; 16 mm.; silent and color. Procurable from Abbott Laboratories, N. Chicago, Ill.

The Heart Beat Mechanism in Health and Disease (1933) (By Clayton J. Lundy, M.D., Chicago, Illinois). 11 reels; 16 mm.; silent. Procurable from American Heart Association, 1775 Broadway, New York 19, New York.

The Fluoroscopic Diagnosis of Cardiac Infarction (1940) (By A. M. Master, M.D., A. Grishman, M.D., S. Dack, M.D., H. L. Jaffe, M.D. and R. Gubner, M.D., New York). 1 reel; 16 mm.; silent. Procurable from American Heart Association, 1775 Broadway, New York 19, New York.

Defibrillation of the Heart (1949). 1 reel; 16 mm.; silent and color. Procurable from Claude S. Beck, M.D., 2065 Adelbert Road, Cleveland 6, Ohio.

Division of Patent Ductus Arteriosus (1947) (By John C. Jones, M.D., Los Angeles). 1 reel; 16 mm.; silent and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

Coarctation of the Aorta—Demonstration of Anatomy, Physiology and Surgical Treatment (1948) (By John C. Jones, M.D., Los Angeles, California). 2¼ reels; 16 mm.; sound and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

Coarctation of the Aorta (1948). 1 reel; 16 mm.; silent and color. Procurable from O. Theron Clagett, M.D., Mayo Clinic, Rochester, Minnesota.

Pericardial Resection for Constrictive Pericarditis (1945) (By Richard H. Overholt, M.D., Boston, Massachusetts). 2¼ reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Pericardiectomy for Chronic Cardiac Compression Due to Constricting Pericarditis (1948). 2 reels; 16 mm.; silent and color. Procurable from R. A. Griswold, M.D., Department of Surgery, Louisville General Hospital, Louisville 8, Kentucky.

Partial Pericardiectomy and Epicardiectomy for Calcified Constricting Pericardium (1940). 1 reel; 16 mm.; silent and color. Procurable from Stuart W. Harrington, M.D., Rochester, Minnesota.

Angina Pectoris. A Summary of Objective Studies (1942) (By Joseph E. F. Riseman, M.D., Boston, Massachusetts). 6 reels; 16 mm.; sound and color. Procurable from Harvard Film Service, Inc., 421 Washington St., Somerville 43, Mass.

The Effects of Metallic Ions and Osmotic Disturbances on the Heart (1945) (By K. G. Wakim, M.D., Ph.D., Bloomington, Indiana). 1 reel; 16 mm.; sound. Procurable from Audio-Visual Center, Indiana, University, Bloomington, Indiana.

Aortic Pulmonary Anastomosis for Pulmonary Stenosis (1948) (By Willis J. Potts, Chicago, Illinois). 2 reels; 16 mm.; silent and color. Procurable from Mervin W. LaRue, Inc., 159 E. Chicago Ave., Chicago 11, Illinois.

Cardiotomy (1949) (By Raymond W. McNealy, M.D., Chicago, Illinois). ¾ reel; 16 mm.; silent. Procurable from Mervin W. LaRue, Inc., 159 East Chicago Avenue, Chicago 11, Illinois.

Surgical Division of the Patent Ductus Arteriosus (1949) (By Willis J. Potts, M.D., Chicago, Illinois). 1½ reels; 16 mm.; silent and color. Procurable from Mervin W. LaRue, Inc., 159 E. Chicago Avenue, Chicago 11, Illinois.

Oxygen Therapy in Heart Disease (Produced in cooperation with the American Heart Association) (1946). 3 reels; 16 mm.; sound. Procurable from The Linde Air Products Company, 30 East 42nd Street, New York 17, New York.

Surgical Treatment of a Congenital Heart Disease Pulmonary Stenosis (1948) (By Ralph Adams, M.D. and Harold F. Berg, M.D., Louisville, Kentucky). 2 reels; 16 mm.; silent. Procurable from Louisville General Hospital, Surgical Department, Louisville, Kentucky.

Congenital Cardiovascular Anomalies Amenable to Surgery (1948) (By Stanley Gibson, M.D., Chicago, Illinois). 2¾ reels; 16 mm.; sound. Procurable from Mead Johnson & Company, Evansville 21, Indiana.

Ligation of Patent Ductus Arteriosus (1948) (By Alton Ochsner, M.D., New Orleans). 1¼ reels; 16 mm.; silent and color. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

Pericardial Coelomic Cyst (1948) (By Alton Ochsner, M. D., New Orleans). 1½ reels; 16 mm.; color and silent. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

CARDIOVASCULAR SYSTEM *(Continued)*

Surgical Treatment for Patent Ductus Arteriosus (1950) (By George Humphreys II, M.D., New York City). 1 reel; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York.

Electrocardiography (1949). ¾ reels; 16 mm.; sound and color. Procurable from United States Army.

The Mechanism of the Heart Beat and Electrocardiography (1932) (By Lewis M. Hurxthal, M.D., Boston). 2 reels; 16 mm.; silent. Procurable from Worcester Film Corp., 131 Central Street, Worcester, Massachusetts.

The Use of Digitalis in Heart Failure (1948). 3 reels; 16 mm.; sound and color. Procurable from Wyeth Inc., 1600 Arch Street, Philadelphia 3, Pennsylvania.

Coarctation of the Aorta—Demonstration of Anatomy Physiology and Surgical Treatment (1948) (By John C. Jones, M.D., Los Angeles). 2¼ reels; 16 mm.; sound and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

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Surgical Treatment for Congenital Pulmonary Valvular Stenosis (1950) (By George H. Humphreys II, M.D., New York City). 20 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $75; Rental $6).

Mitral Commissurotomy (1952) (By John L. Madden, M.D., New York City). 20 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $75; Rental $6).

Congenital Pulmonary Stenosis with Intact Interventricular Septum (By Willis J. Potts, M.D., William L. Riker, M.D. and Stanley Gibson, M.D., the Children's Memorial Hospital, Chicago). 24 mins.; 16 mm.; silent and color. Procurable from Mervin W. LaRue, Inc., 159 East Chicago Avenue, Chicago 11, Illinois.

ESOPHAGUS

Transthoracic Resection of Esophagus—Lower Third for Carcinoma (1946) (By Ralph Adams, M.D., Boston). 2 reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Epiphrenic Esophageal Diverticulectomy (1940). ¾ reel; 16 mm.; silent and color. Procurable from Howard H. Drake, M.D., 511 South Bonnie Street, Los Angeles 5, California.

Pedunculated Multiple Myxofibromata of the Upper Esophagus (1941). 1 reel; 16 mm.; silent and color. Procurable from Stuart W. Harrington, M.D., Rochester, Minnesota.

Pedunculated Polypoid Lipoma Originating at Introitus of Esophagus and Extending to Cardia (1944). 1 reel; 16 mm.; silent and color. Procurable from Stuart W. Harrington, M.D., Rochester, Minnesota.

Pulsion Diverticulum of Lower Esophagus (Transpleural one-stage diverticulectomy) (1948). 1 reel; 16 mm.; silent and color. Procurable from Stuart W. Harrington, M.D., Rochester, Minnesota.

Diseases of the Esophagus (1949) (By Paul H. Holinger, M.D., Chicago). 1¾ reels; 16 mm.; silent and color. Procurable from The Jacques Holinger Memorial Fund, 700 North Michigan Avenue, Chicago 11, Illinois.

ESOPHAGUS *(Continued)*

Congenital Atresia of the Esophagus with Tracheo-Esophageal Fistula. Surgical Repair (1949) (By W. D. Seybold, M.D., Rochester). 1½ reels; 16 mm.; silent and color. Procurable from Motion Picture Film Library, Mayo Clinic, Rochester, Minnesota.

Esophagogastrostomy for Achalasia of the Esophagus (1949) (By John L. Madden, M.D., New York City). 2½ reels; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46st Street, New York 17, New York.

The Surgical Treatment for Carcinoma of the Lower End of the Esophagus (1947). 3 reels; 16 mm.; silent and color. Procurable from Philip Thorek, M.D., 25 East Washington Street, Chicago 2, Illinois.

Cervical Diverticulectomy (One stage operation) (1948). 1¾ reels; 16 mm.; silent and color. Procurable from Philip Thorek, M.D., 25 East Washington Street, Chicago 2, Illinois.

Supra-Aortic Esophagogastrostomy for Carcinoma of the Midportion of the Esophagus (1948). 2¼ reels; 16 mm.; silent and color. Procurable from Philip Thorek, M.D., 25 East Washington Street, Chicago 2, Illinois.

Transthoracic Esophageal Diverticulectomy (1948). 1½ reels; 16 mm.; silent and color. Procurable from Philip Thorek, M.D., 25 East Washington Street, Chicago 2, Illinois.

Resection of Vagus Nerves Trans-Thoracic Approach (1949) (By John L. Madden, M.D., New York City). 16 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $125; Rental $8.50).

Transthoracic Esophagogastrectomy for Carcinoma of the Lower Esophagus (1948) (By R. Arnold Griswold, M.D., Louisville). 1½ reels; 16 mm.; silent. Procurable from Department of Visual Education, Louisville General Hospital, 323 East Chestnut Street, Louisville 2, Kentucky.

Operation for Spontaneous Rupture of the Esophagus (1951). 1¾ reels; 16 mm.; silent and color. Procurable from S. Allen Mackler, M.D., 104 South Michigan Ave., Chicago 3, Illinois.

Transthoracic Resection for Carcinoma of the Cardiac End of the Stomach (1946) (By Herbert H. Hawthorne, M.D., Philadelphia). 2 reels; 16 mm.; silent and color. Procurable from University of Pennsylvania, 19th and Lombard Streets, Philadelphia, Pennsylvania.

RESPIRATORY SYSTEM

Upper Selective Thoracoplasty for Pulmonary Tuberculosis (1946) (By Richard H. Overholt, M.D., Boston). 1¾ reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Surgical Extirpation of Intrathoracic Tumor (1938) (By Frank S. Dolley, M.D. and John C. Jones, M.D., Los Angeles). 1 reel; 16 mm.; silent and color. Procurable from Frank S. Dolley, M.D., 427 South Arden Blvd., Los Angeles, California.

Crushing Injuries of the Thorax. The Treatment of Hemopneumothorax by Temporary Closed Suction Drainage and Pulmonary Decortication (1946) (By Howard K. Gray, M.D. and Robert W. Gentry, M.D., Rochester). 1½ reels; 16 mm.; silent and color. Procurable from Howard K. Gray, M.D., Rochester, Minnesota.

Hydatid Cyst of the Chest (1944) (By Harold Brunn, M.D., San Francisco). 1 reel; 16 mm.; silent and color. Procurable from Thoracic Surgery Department, University Hospital, The Medical Center, San Francisco 22, California.

Left Lower Lobectomy for Bronchiectasis (1945) (By Richard H. Overholt, M.D., Boston). 1½ reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Left Upper Lobectomy (1945) (By Richard H. Overholt, M.D., Boston). 2 reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Right Pneumonectomy for Primary Carcinoma of the Lung (1946) (By Richard H. Overholt, M.D., Boston). 1¼ reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Lobectomy and Segmental Resection for Bilobar Bronchiectasis (1947) (By Ralph Adams, M.D., Woodbury). 1¾ reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

RESPIRATORY SYSTEM *(Continued)*

Segmental Pulmonary Resection for Multilobar Bronchiectasis (1948) (By Richard H. Overholt, M.D., Reeve H. Betts, M.D. and Francis M. Woods, M.D., Boston). 2 reels; 16 mm.; silent and color. Procurable from Davis & Geck, 57 Willoughby Street, Brooklyn 1, New York.

Pulmonary Resection for Bronchial Adenoma (1948). 2 reels; 16 mm.; silent and color. Procurable from Alfred Goldman, M.D., 416 North Bedford Drive, Beverly Hills, California.

Bronchoscopic Cinematography of Bronchial Tumors (1945) (By Paul H. Holinger, M.D. and Ralph G. Rigby, M.D., Chicago). 1 reel; 16 mm.; silent and color. Procurable from The Jacques Holinger Memorial Fund, 700 North Michigan Ave., Chicago 11, Illinois.

A Bronchoscopic Clinic in Kodachrome (1949) (By Paul H. Holinger, M.D., Kenneth C. Johnston, M.D. and Frank J. Novak III, M.D., Chicago). $1\frac{3}{4}$ reels; 16 mm.; silent and color. Procurable from The Jacques Holinger Memorial Fund, 700 North Michigan Ave., Chicago 11, Illinois.

Unilateral Total Pneumonectomy for Bronchogenic Carcinoma (1944) (By Alton Ochsner, M.D., New Orleans). $1\frac{3}{4}$ reels; 16 mm.; silent and color. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

Lobectomy for Chronic Lung Abscess (1948) (By Alton Ochsner, M.D., New Orleans). $2\frac{1}{4}$ reels; 16 mm.; silent and color. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

Teratoma of Lung (1944) (By Harold Brunn, M.D., San Francisco). 1 reel; 16 mm.; silent and color. Procurable from E. R. Squibb & Sons, 745 Fifth Avenue, New York, New York.

Extrafascial Lucite Plombage for Pulmonary Tuberculosis (1949). 2 reels; 16 mm.; silent and color. Procurable from Alfred Goldman, M.D., 416 North Bedford Drive, Beverly Hills, California.

Decortication of the Unexpandable Pneumothorax Lung. 1 reel; 16 mm.; silent and color. Procurable from David H. Waterman, M.D., Medical Arts Building, Knoxville, Tennessee.

Technique of BCG Vaccination (Part I: Tuberculin Testing) (Part II: BCG Vaccination). 40 mins.; 16 mm.; sound and color. Procurable from Communicable Disease Center, U. S. Public Health Service, P. O. Box 185, Chamblee, Georgia (Loan).

Excision Tuberculoma, Right Lower Lobe, and Thoracolumbar Sympathectomy (Armed Forces Institute of Pathology Medical Illustration Service with Signal Corps, U. S. Army). 10 mins.; 16 mm.; sound and color. Procurable from Commanding General, Attention: Surgeon, Headquarters, First to Sixth Army (According to location of user).

Lobectomy, Right Upper and Middle Lobes, In the Treatment of Pulmonary Tuberculosis (Armed Forces Institute of Pathology, Medical Illustration Service, with Signal Corps, U. S. Army). 22 mins.; 16 mm.; sound and color. Procurable from Commanding General, Attention: Surgeon, Headquarters, First to Sixth Army (According to location of user).

Thoracoplasty, First Stage and Second Stage, in the Treatment of Pulmonary Tuberculosis (Armed Forces Institute of Pathology, Medical Illustration Service, with Signal Corps, U. S. Army). 23 mins.; 16 mm.; sound and color. Procurable from Commanding General, Attention: Surgeon, Headquarters, First to Sixth Army (According to location of user)

Gram's Stain—A Demonstration of the Technic (1950) (Produced under the direction of Harry E. Morton, Sc.D., University of Pennsylvania. Sponsored by the Committee on Materials for Visual Instruction in Microbiology of the Society of American Bacteriologists). 9 mins.; 16 mm.; sound and color. Procurable from Sturgis-Grant Productions, Inc., 314 East 46th Street, New York 17, New York (Sale $75; Rental $6).

Bronchiogenic Carcinoma (1951) (Directed by Brian Blades, M.D., Washington, D. C. Advisory Committee: William E. Adams, M.D., Paul H. Holinger, M.D., John C. Jones, M.D. and Alton Ochsner, M.D.). $1\frac{1}{2}$ reels; 16 mm.; sound and color. Procurable from Chief Medical Director, Veterans Administration, Vermont Avenue and H Street, N. W., Washington 25, D. C.

Diaphragmatic Hernia (1949) (By J. Norman O'Neill, M.D., Los Angeles). 1 reel; 16 mm.; silent and color. Procurable from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36, California.

RESPIRATORY SYSTEM *(Continued)*

Diseases of the Ear, Nose and Throat (1947) (By Paul H. Holinger, M.D., Chicago). 2 reels; 16 mm.; silent and color. Procurable from The Jacques Holinger Memorial Fund, 700 North Michigan Avenue, Chicago 11, Illinois.

The Endoscopic Appearance of Diseases of the Trachea (1951) (By Paul H. Holinger, M.D. and Kenneth C. Johnston, M.D., Chicago). 1½ reels; 16 mm.; silent and color. Procurable from The Jacques Holinger Memorial Fund, 700 North Michigan Avenue, Chicago 11, Illinois.

Needle Biopsy of the Lung (1950). 1 reel; 16 mm.; silent and color. Procurable from George P. Rosemond, M.D., 3401 North Broad St., Philadelphia 40, Pennsylvania.

Laboratory Diagnosis of Influenza. 17 mins.; 16 mm.; sound. Procurable from United World Films, 1445 Park Avenue, New York 29, New York.

Surgery in Chest Diseases (Prepared in 1943 for the British Ministry of Information, London, England. Produced by G. B. Instructional, Ltd., London). 1 reel; 16 mm.; sound. Procurable from American Medical Association, Committee on Medical Motion Pictures, 535 North Dearborn Street, Chicago 10, Illinois.

Laboratory Diagnosis of Tuberculosis. Parts I, II, and IV (1949). Part I: Preparation of a Culture Medium. Part II: Preparation of Sputum Specimens. Part III: In production. Part IV: Typing of Tubercle Bacilli by Animal Inoculation. Part I, 14 mins.; Part II, 16 mins.; 16 mm.; sound. Procurable from U. S. Public Health Service, Communicable Disease Center, 605 Volunteer Bldg., Atlanta, Georgia (Loan).

HOSPITAL PERSONNEL

The Air We Breathe (The Story of Respiratory Protection for the Worker) (1948). 2¼ reels; 16 mm.; sound. Procurable from Mine Safety Appliance Co., Braddock, Thomas and Meade Sts., Pittsburgh 8, Pennsylvania.

Oxygen Therapy Procedures (Illustrates different types of oxygen therapy apparatus and demonstrates correct operating procedures) (1944). 3 reels; 16 mm.; sound. Procurable from The Linde Air Products Company, 30 East 42nd Street, New York 17, New York.

Occupational Therapy in Tuberculosis (Produced in 1949 by the U. S. Army). 27 mins.; 16 mm.; sound. Procurable from The Army Surgeon of the Army area in which the request originates (Loan).

LAITY

The Air We Breathe (The story of respiratory protection for the worker (1948). 2¼ reels; 16 mm.; sound. Procurable from Mine Safety Appliances Company, Braddock, Thomas and Meade Sts., Pittsburgh 8, Pennsylvania.

Tuberculosis (1945). 1 reel; 16 mm.; sound and color. Procurable from Institute of Inter-American Affairs, 499 Pennsylvania Avenue, N. W., Washington, D. C.

This is TB (1946). 1 reel; 16 mm.; sound. Procurable from National Tuberculosis Association.

You Can Lick TB (1950). 21 mins.; 16 mm.; sound. Procurable from Presentation Division, Veterans Administration, Washington, D. C. (Loan).

MISCELLANEOUS

Chonechondrosternon (1949) (By Alton Ochsner, M.D., New Orleans). 1¾ reels; 16 mm.; silent and color. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

Resection of a Large Thymic Tumor (1946) (By Alton Ochsner, M.D., New Orleans). 2¼ reels; 16 mm.; silent and color. Procurable from Alton Ochsner Medical Foundation, 3503 Prytania Street, New Orleans 15, Louisiana.

Thymectomy for Myasthenia Gravis (1950). 1 reel; 16 mm.; silent and color. Procurable from Alfred Goldman, M.D., 416 North Bedford Drive, Beverly Hills, California.

The Medical Motion Picture; Its Development and Present Application (1947). 2¾ reels; 16 mm.; sound and color. Procurable from American Medical Association, Committee on Medical Motion Pictures, 535 North Dearborn Street, Chicago 10, Illinois.

COMMITTEE

Paul H. Holinger, Chicago, Illinois, Chairman
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Obituaries

MINAS JOANNIDES

1895 - 1952

On September 8, 1952, after an illness of about three years, Dr. Minas Joannides died at Grant Hospital, Chicago, Illinois, of myocardial infarction at the age of 57.

Dr. Joannides was one of the three incorporators of the American College of Chest Physicians and served as the College Treasurer from 1947 to the time of his death. In addition, he was a charter member and Past President of the Illinois Chapter and held Chapter offices and many important committee appointments in the Chapter and in the National Organization. By his passing, the College has lost a devoted member and a tireless worker and teacher in the field of thoracic surgery.

Dr. Joannides was born in Nazly, Turkey, on February 15, 1895. He completed his preliminary education at Milwaukee, Wisconsin where he graduated from the West Division High School in 1915. He took his pre-medical and part of his medical work at the University of Wisconsin. The remainder of his medical schooling was done at Washington University Medical School, St. Louis, Missouri, where he graduated in 1921. While attending Medical School, he did graduate work in Physiology under Dr. Joseph Erlanger at Washington University Medical School and served as an interne at Barnes Hospital 1921-1922 under Dr. Evarts A. Graham.

Following this, he served as an instructor in Surgery at the University of Minnesota 1922-1925 and was elected to membership in Sigma Xi in Surgery, Minneapolis Chapter in 1925. After completion of his work at the University of Minnesota, he came to Chicago and served as an assistant in surgery at Rush Medical College from 1926-1927 and did graduate work in surgery under Dr. Carl A. Hedblom. Under Dr. Hedblom he obtained his Master of Science degree in Surgery in 1928. In 1929 he did research work in lung pathology under Professor Max Busch in Berlin, Germany.

He became a Fellow of the American College of Surgeons in 1930 and was appointed Associate in Surgery at the University of Illinois with the rank of Clinical Associate Professor of Surgery. He served as Dispensary Physician, Chicago Municipal Tuberculosis Sanatorium 1926-1927 and did special research work on pneumothorax therapy. He was the Director of the Collapse Therapy Clinic for the Municipal Tuberculosis Sanitarium from 1934-1940.

Dr. Joannides was an active member of the American Association for Thoracic Surgery, Treasurer and Past President of the Chicago Tuberculosis Society, a member of the Illinois Academy of Science, National Tuberculosis Association, Chicago Medical Society and American Medical Association.

He was a veteran of World War I, having served in the U. S. Army and was a past commander of the Hellenic Post of the American Legion. He was also a member of the Masonic Bodies, including the Scottish Rite and Shrine.

Dr. Joannides was the author of over 50 original articles, dealing with many facets of diseases of the chest. Recently he completed two chapters in the College book, now in press, entitled "Non-Tuberculous Diseases of the Chest." He served

as Thoracic Surgeon at Columbus Hospital, Illinois Masonic Hospital, Grant Hospital, St. Bernards, Alexian Brothers, St. Mary of Nazareth and was consulting thoracic surgeon to the Oak Forest Tuberculosis Hospital and the U. S. Public Health Service.

He is survived by his wife, Laura, a daughter, Annette, a son, Dr. Minas Jr. and a grandson Minas III.

His devoted interest and untiring participation in College affairs was an inspiration to others to contribute their best efforts to the cause of the College. To those of us who knew him well, he will long be remembered for his splendid leadership and his constant willingness to share with others the knowledge and wisdom which he had gathered from his extensive practice in research work.

Darrell H. Trumpe, M.D., Governor for Illinois.

PAUL E. PIFER
1895 - 1952

Paul E. Pifer of Kenosha, Wisconsin, died on September 7, 1952, following a long illness. He was born in Reynoldsville, Pennsylvania. He graduated from the Medical School of Western Reserve University, in 1932. He completed his internship and surgical residency in Cleveland, Ohio, and opened his office in Kenosha, Wisconsin in 1934. His professional affiliations included Willowbrook Sanatorium and St. Catherine and Kenosha Hospitals, Kenosha, Wisconsin. He held the position of Medical Director of the Willowbrook Sanatorium from 1944 to 1951 when he retired because of ill health.

He was a man of great personal charm and of high professional integrity. His indefatigable, unselfish devotion to the care and treatment of his patients elicited the highest praise from the public as well as from his fellow practitioners of medicine.

His passing is a great loss to the Wisconsin Medical profession in general and to the Wisconsin Chapter of the College in particular.

Alfred A. Busse, M.D., Governor for Wisconsin.

MOSES J. STONE
1895 - 1952

Dr. Moses J. Stone, one of the Regents and founders of the American College of Chest Physicians and very active in the affairs of tuberculosis in New England, died very suddenly at the age of fifty-seven, at the Beth Israel Hospital in Boston on December 13, 1952.

Dr. Stone was synonymous with tuberculosis in Boston since he first became interested in the disease after graduating from Tufts Medical School in 1921. He obtained his tuberculosis training at the Rutland State Sanatorium and developed into one of the leading authorities in the tuberculosis field.

He was one of the founders of the Jewish Tuberculosis Sanatorium of New England at Rutland, Massachusetts and remained Physician-in-Chief until his death. He has been chief of the Thoracic Clinic at the Beth Israel Hospital in Boston for many years. He was assistant-visiting physician at the Massachusetts Memorial Hospital and was very active in the tuberculosis clinics in the Boston Health Department for more than twenty-five years. He was Assistant Professor in Medicine at Boston University School of Medicine and Instructor in Medicine at Tufts Medical School.

Dr. Stone was a very familiar figure at all the medical meetings and conventions where his strong, forceful personality was so brightly displayed. He delivered many papers on tuberculosis and was an eagerly sought speaker on many occasions

both in medical and lay affairs. He was author of a recent text book "Diagnosis and Treatment of Pulmonary Tuberculosis." He remained very active until the very last in his chosen field.

Dr. Stone's devotion to his patients was that of a father to his children. He gave unsparingly of his energies. He was loved alike by his patients and associates.

At his funeral services there were throngs of people from all walks of life, and representing every race and creed, which testified to the affection in which he was held by this community.

We here in New England have indeed suffered a great loss in his passing. Dr. Stone is survived by his wife, Miriam C. Stone and three children, Elhanan, Harris and Syril Anne.

Francis M. Woods, M.D., Governor for Massachusetts.

HARRY FLOYD RAPP
1888 - 1952

Dr. Harry Floyd Rapp, age 64, widely-known physician and leader in the fight against tuberculosis, died in the University Hospital, Columbus, Ohio, of leukemia.

He had practiced medicine in Scioto County and Portsmouth about 40 years. He was graduated from Portsmouth High School in 1907 and the College of Medicine at the University of Cincinnati in 1911. He served his internship at Deaconess Hospital, Cincinnati. Dr. Rapp served during World War I as a captain in the medical corps with Ohio's 37th Infantry Division. A member of the Masonic lodge and the American Legion, he was active in the work of the Scioto County Tuberculosis and Health Association. He was the prime mover in organization of community groups to fight for control of tuberculosis. He also was active in the Ohio Public Health Association, which he served as president in 1925, and the Hempstead Academy of Medicine, now named the Scioto County Medical Society. He served as chief of staff of Mercy Hospital in 1929 and again from 1939 to 1942. He was secretary-treasurer of the hospital's medical staff from 1929 to 1932.

He is survived by his wife and four children. The medical profession has lost a worthy member and will long be remembered for his magnificant work in the medical world.

David W. Heusinkveld, M.D., Governor for Ohio.

Book Reviews

Modern Practice in Tuberculosis. Edited by T. Holmes Sellors, M.A., D.M., M.Ch., F.R.C.S., Thoracic Surgeon, Middlesex Hospital; Surgeon, London Chest and Harefield Hospitals; Teacher of Surgery, Middlesex Hospital Medical School and the Institute of Diseases of the Chest, University of London, and J. L. Livingstone, M.D., F.R.C.P., Physician, King's College Hospital and Brompton Hospital, London; Fellow of King's College, University of London; Teacher of Medicine, King's College Hospital Medical School and the Institute of Diseases of the Chest, University of London. Volumes I and II. Butterworth and Company (Publishers), Ltd., Bell Yard, Temple Bar, London, 1952. Distributors in U.S.A., Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, New York. Price $25.00.

This work in two volumes is composed of thirty-nine chapters by as many authors, each a recognized authority in the subject presented. These chapters were brought together by the two editors, Drs. Sellors, thoracic surgeon, and Dr. Livingstone, internist, both of whom are favorably and widely known for their fine practical work in leading London hospitals. An excellent introduction was prepared by Dr. S. R. Gloyne who died shortly before the volumes were published.

There is little in the entire field of tuberculosis that is not covered in these two volumes. Bacteriology, pathology, laboratory methods of investigation, rehabilita-

tion immunity, x-ray, drugs, psychology, are some of the subjects included in Volume I. Dr. R. R. Trail has an excellent chapter on the colony for the tuberculous patient.

Volume II is devoted largely to clinical aspects although the first chapter pertains to primary tuberculosis. In this volume various surgical procedures are discussed. Chapters are included on extrathoracic tuberculosis including the skin, the pericardium, the eyes, genito-urinary system, bones and joints, lymphatic system and the abdominal organs. Probably many readers would have greatly appreciated a chapter on the bovine type of tuberculosis. Some of the subjects discussed in these volumes are highly controversial which lends great interest.

Both volumes are profusely illustrated with excellent reproductions, especially of roentgenograms. Each volume contains a splendid index.

Physicians especially interested in tuberculosis and closely allied subjects will be rewarded by reading these volumes. To others they will be valuable as a reference work and therefore should be placed in all medical libraries.

Tuberculosis. By Saul Solomon, M.D., Coward-McCann, Inc., publisher, New York, 1952. Pp. 286, Price $3.50.

The purpose of this book as stated by the author is to present to the general reader the current knowledge and recent advances in the field of tuberculosis. The author has done this in a general way in a very scholarly, factual and interesting manner. It is a book which health workers will find very helpful easy reading. Many patients will find it a contribution to their understanding. Some patients may find it difficult to read because of details as they are interested only in the essential facts that have a direct bearing on their recovery.

While rest is repeatedly referred to as important in treatment the position of rest as the basic therapeutic principle should have greater emphasis. Rest for a tuberculous patient should be defined. The distinction between bed rest and rest in bed should be clarified. The influence of treating the patient as an individual, as well as the influence of the environment of the patient, in enabling the patient to rest is not adequately stressed. There is a lack of appreciation of the part sanatorium life plays in the long time mental and physical rehabilitation of the patient.

Extrapulmonary tuberculosis and tuberculosis among veterans is briefly discussed. There is a chapter ably devoted to the controversial subject of BCG, to bovine tuberculosis and to a program for eradicating tuberculosis.

Edward W. Hayes.

COURSES IN LABORATORY DIAGNOSIS IN TUBERCULOSIS

The Division of Chronic Disease and Tuberculosis, Public Health Service, the Bacteriology Laboratories of the Communicable Disease Center, Chamblee, Georgia, will offer two courses in the laboratory diagnosis of tuberculosis on the following dates: *March 16-27, 1953* and *November 16-27, 1953*.

Additional information and applications may be obtained from Laboratory Training Services, Communicable Disease Center, Public Health Service, P. O. Box 185, Chamblee, Georgia.

COLLEGE EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

19th Annual Meeting, American College of Chest Physicians, Hotel New Yorker, New York City, May 28-31, 1953.

Interim Session, Semi-Annual Meeting, Board of Regents, St. Louis, Missouri, November 29-30, 1953.

20th Annual Meeting, American College of Chest Physicians, San Francisco, California, June 17-20, 1954.

3rd International Congress on Diseases of the Chest, Barcelona, Spain, Fall of 1954.

POSTGRADUATE COURSES

Postgraduate Course, Diseases of the Chest for General Practitioners, Milwaukee, Wisconsin, March 4, 11, 18, 25, 1953.

6th Annual Postgraduate Course on Diseases of the Chest, Philadelphia, Pennsylvania, March 23-27, 1953.

8th Annual Postgraduate Course on Diseases of the Chest, Chicago, Illinois, September 28-October 1, 1953.

6th Annual Postgraduate Course on Diseases of the Chest, Hotel New Yorker, New York City, November 2-6, 1953.

CHAPTER MEETINGS

Potomac Chapter Meeting, White Sulphur Springs, West Virginia, April 10, 1953.

Florida Chapter Meeting, Hollywood, Florida, April 26, 1953.

Missouri Chapter Meeting, Hotel President, Kansas City, Missouri, April 26, 1953.

Ohio Chapter Meeting, Hotel Gibson, Cincinnati, Ohio, April 22, 1953.

Oklahoma Chapter Meeting, Mayo Hotel, Tulsa, Oklahoma, April 12, 1953.

Texas Chapter Meeting, Houston, Texas, April 26-29, 1953.

13th Annual Meeting, New York State Chapter, Hotel Statler, Buffalo, New York, May 7, 1953.

MEDICAL SERVICE BUREAU

POSITIONS WANTED

Male Tuberculosis Specialist seeks position with institution. Experienced in collapse therapy, thoracoscopy, bronchoscopy, radiology, and BCG. Canadian citizen. Please address all inquiries to Box 268B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Male physician, 52, Canadian graduate, passed Alabama State Boards, seeks residency in tuberculosis hospital or sanatorium. Served as resident in Canadian tuberculosis hospital for 3 years. Please address inquiries to Box 269B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Male physician, F.C.C.P., Georgetown University graduate, age 36, married, 4 children, now in service with the U. S. Army, will be released in August 1953, desires position in California. Experienced in TB. Please address Box 270B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11 Illinois.

Canadian chest physician, F.R.C.P., F.A.C.P., and F.C.C.P., seeks responsible position. Highly trained in general internal medicine as well as tuberculosis and other diseases of the chest. Wide research experience and numerous publications. Also widely experienced in sanatorium administration. Research facilities and university affiliation are desired. Please address all inquiries to Box 271B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Thoracic and general surgeon, woman, M.D., M.S. Teaching, research, and practical experience. Interested in United States or foreign location. Please include particulars in reply. Please address all inquiries to Box 272B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Thoracic and general surgeon, board eligible, age 44. Several years experience and training in tuberculosis. Teacher in different medical schools. New York State license. Desires hospital or sanatorium appointment. Please address all inquiries to Box 273B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

POSITIONS AVAILABLE

Assistant Medical Director wanted for 200 bed Tuberculosis Hospital, approved by American College of Surgeons. Applicant must have experience in tuberculosis field and be eligible for Michigan license. Excellent salary and generous fringe benefits offered. Please address Box 261A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Resident Physician wanted. Tuberculosis experience essential. Call or write Deborah Sanatorium, Browns Mills, New Jersey.

Physician with some experience in collapse therapy for private clinic in Detroit. Good salary and eventual partnership. Should be eligible for Michigan license. Please address Box 262A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

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Ritter J. S. and Bloomberg, H.: J. Urology 1952, 67, 543-546.

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